Introduction and overview of precision medicine

Hi, everybody. Welcome. It's great here to have Dr. Craig Tannehill from Wrestling Health in Hollywood, Florida. Always great to talk to Craig. And he's done such a fantastic job and had some wonderful results.

And I just thought it would be helpful to all of us to hear about some of his techniques, some of his tips for best outcomes for patients with cognitive decline.

So Craig, welcome. Thank you so much for joining us. Thanks, Dale. Thanks for having us there. Could you talk a little bit about how long you have been dealing with people with cognitive decline and some of the features that you feel have helped the most?

Yeah. So we've been working on implementing precision medicine for cognitive decline for about six years now. And, you know, I think we've learned a lot over the years in doing this.

I think first is just really having clarity about what we're trying to do. And, you know, how I tell patients now what we're doing is we're really doing precision medicine, you know, guided by a very thorough evaluation of patients, including relative biomarkers, genomics, metabolomics, transcriptomics.

We're implementing multimodal personalized interventions and using a foundation of lifestyle interventions to anchor that. And then finally, we're trying to really practice, you know, one medicine that's really personalized around the individual and using both biomarkers and sort of excitingly now the EEG to guide interventions whenever possible.

And, you know, and we found that implementation is really critical in in helping patients with cognitive disorders. And so we've tried to divide that into really five components of implementation.

You know, one is around the tools and the frameworks used to manage implementation. The second is the team, the multidisciplinary team that's part of the patient care in our case, we have a physician, nurse practitioner, health coach, dietician, exercise trainer and indoor environmental professional.

That's all working together. We try to really get the approach right with the patients specifically around trying to get traction in the first three or six months so that they can see results.

And that really does create the right hope and the right psychology. We're using an evidence informed approach, not an evidence based approach on how to incorporate new evidence and protocols.

And as you know, there's so much new evidence that coming in year by year that we have to really stay on top of what's happening.

Implementation strategies and clinical workflow

And then finally, I think having a good understanding of the prognosis and likely response upfront, I think all of those things really guide implementation and know some of the things that we've learned is, you know, around the tools and frameworks.

This can become a process where you're literally following dozens of biomarkers. And so you have to have systems to keep those biomarkers and, you know, organized and in place.

And we've kind of done a lot of that just on Excel and having organization. But we kind of have the internal spreadsheet that says, now here are 55 different potential root causes here.

The biomarkers you follow here, here's potential interventions. So that our whole staff really has clarity about what we're trying to do. And then we've kind of have a view of how much how easy it is to do certain things, how expensive it is, and where the benefit is, and to really try to sequence these things and so that the patients get the optimal care and so, you know, some of the lessons we've learned is that getting the treatment of trophic factors and getting the lifestyle upfront is really critical.

So really hold off of treatment of toxins and infections until later, you know, but also understand what the patients can do. And so it's really key to not overload the patients.

And everybody's coming from a different place. But and sometimes people really do need intensive interventions upfront. You know, but sometimes it's not necessary.

And so it's all about really personalizing this. And I think we are we are not at the point where this is guideline medicine. You know, this has to be there is a huge art to doing this. And and, you know, I think we've also been very, you know, collaborative with other people.

We don't see any of this as being proprietary. It's rather we're all part of a network and community practitioners that are trying to get the right answer.

And so, you know, we want to get the right answer. Sometimes it's us doing it, sometimes it's other people helping out with interventions, you know? And so we really want to have a collaborative approach.

And, you know, we've noticed over the years that this is more like surgery than medicine. As you said, there's a tremendous art to this. And therefore, it should probably come as no surprise that, you know, many physicians are not getting such good results and other physicians are getting fantastic results.

And it really depends on how you evaluate the patient, what you do in what sequence, how you figure out what's going wrong. And we see this again and again and again.

And so maybe you could talk about, you know, one recent example of success. Right. Absolutely. So I think this is a case, I think where it says somebody who really, I think, taught us how much neuroplasticity is achievable.

And, you know, and and and again, another theme about how toxins and toxicants can really be at the root cause of so many of these issues. This is a woman who was in her mid-fifties who came to us about three years ago with cognitive issues, word finding, focus and concentration.

She had multiple, multiple symptoms. Her MSC was in the one fifties. She had a lot of limbic system and gut issues, very bad sleep headaches and joint inflammation and our hands and wrists.

She did have a history of having now breast implants for about 25 years and had a redo about five years ago where there was no prob problem with leakage or encapsulation.

And then when we evaluated her, we found that she was with three and four. She had really elevated innate immune system markers across the board. Her neuro quant showed significant atrophy, sort of her cortical gray was in the third percentile.

And and then her cognitive testing, her CNS Vitus us was in the 15th percentile and the attention was in the fourth percentile. And we did sort of advanced toxicant testing company and Germany called IGF.

And what's unique about them is you're actually able to test for the silicone and the breast implants, which most of the US toxins testing doesn't allow you to do.

And so she had very strong, high T-cell reactivity against multiple silicones plus chemicals, metals and molds, and so they were sort of there all across the board.

Yeah. And the key interventions over about a two plus year period was she did get an ex plant of the, of the breast implants. There was a lot, a lot of environmental remediation.

She did get intravenous phosphatidylcholine and detoxification protocols. She did decide to get a hyperbaric oxygen at home, home based treatment as well as a B light that was home based light therapy and neurofeedback.

And, you know, the kind of results that we saw after about a year and a half, we saw sort of almost in the first six months, you know, significant improvement.

But after about a year and a half, her repeat neuro quant showed growth from the cortical gray, went from the third percentile to the 38th percentile.

You know, the frontal lobe was in the third percentile. And that had grown to the 36%, while the temporal lobe grew from the second percentile to the 23rd.

And her CNS burble went from the 15th percent out to the 84th percentile. Wow. So and her miscue went from 124 down to 16. So all of the symptoms kind of went away.

What was really notable is, is that when we did the when the explosion happened, she did not reduce her T-cell reactivity to so accounts for about it required about a year later plus a couple of rounds of detoxification and so but we had objective biomarkers to follow.

Case study: reversing cognitive decline with toxicant removal

And interestingly the IG out showed that the silicones were attached to the DNA and we could actually see the, you know, the decrease of the DNA addict's over over time.

And so you know but really we've we've oftentimes have thought about, you know, a low percentiles on the cortical gray as being a real negative prognostic factor.

And sometimes it's hard to tell upfront, you know, what is really, you know, what the potential is for neuroplasticity. And you can't just use that as as, you know, just one image to to tell that.

But in her case, we were we were very happy with the how much neuroplasticity she was able to show. Yeah, really striking. And I think, you know, all sorts of lessons there, beginning with the fact that, you know, just reversing cognitive decline like that has always been we've always been taught that that's impossible.

And the whole idea of a reverse Alzheimer's summit is like, you know, how do you do that? So most most physicians would say it's not possible. And I think the Alzheimer's Association has said many times in the past that there's nothing that will prevent, reverse or delay Alzheimer's disease.

So I think, you know, this is really an era of change. And here's, you know, yet another wonderful example of someone in striking improvements in the volume metrics.

So that's really exciting. And you mentioned the IGL with with the DNA, ADCs and things like that. Very, very interesting. So now did you with someone like this when they have antibodies, are you using low dose naltrexone as part of your approach or not?

Yeah, we absolutely find that low dose naltrexone is very helpful, you know, in terms of its impact on on microglial cells. She had elevated white matter on on her neuro quanta as well.

And so when we do see that, we oftentimes will see that also in that and the cerebellum will do well. We'll use low dose naltrexone. And she's a good example of what we're calling now, sort of our quantum protocols, which is really an acronym for, you know, QE, AG Monitor, where what's what we have found with the QE G now is that if you can train on it and learn how to use that, it is almost the equivalent of having a pocket ultrasound to basically

look at brain function.

And as long as you subscribe and trained on a software protocol that's not in a service or subscription base, the marginal cost is super low. And and once you see what it can do, it's I don't think you'd ever go back because what it allows you to do the QE, is to get very targeted.

You can see what's going on in the brain and potentially use, you know, laser or neurofeedback or electrical stimulation. What we clearly Sienkiewicz, though, is that we see that there are changes in brainwave functions that happen before the changes in symptoms.

So oftentimes you'll see those changes happen and you can see them quickly within 1 to 2 weeks of treatment, oftentimes depending on what you do. And so that allows us that really the ability of being more precise around around helping a patient.

And then we can kind of see, you know, so much of this is trying to figure out what's the dose response of what you're doing with treatments and where there are synergy.

And and so it's it's giving us at least more objective way of doing this. And I think importantly, it's reducing the pressure on patients to kind of perform on the test.

You know, with that with cognitive testing, there can be a lot of variability, as you know, with stress and anxiety to take the test. And we can kind of look at the QED and say, hey, it looks like things are moving in the right direction.

You don't need to worry about taking the test. You're going to, you know, improve with flying colors. And so we will use that a little bit to time. You know, the cognitive performance testing we want, you know, we redo those tests too often because for multiple reasons.

Yeah. And objective measures of improvement that, as you say, are not related to things like stress so much a huge, huge issue. So I think this is you know, this is so important.

Now on your colleagues, are you mostly interested in dominant alpha rhythm? Are you looking at theta beta ratios? Are you looking at, you know, amplitudes?

What sorts of things are you looking at? So we are taking a pretty holistic approach to that, to the QED. So we definitely are looking at amplitude, but we are also looking at connectivity.

We do see a lot of of mild TBI that's sort of been there in the in the past where you can clearly see the connectivity changes. You clearly have a number of issues oftentimes in younger patients where limbic system Overactivation is clearly present and and then also contributing to cognitive function.

And so, you know, we'll we'll kind of look at everything globally and then put together a protocol. But we've certainly seen that you know, theta beta ratios, certainly when patients come in with severe cognitive impairments, we we'll really see that that and that that stand out.

So yeah, it's a really good point. And, you know, people often talk about interracial cortex as being the first area that's hit by Alzheimer's. But really prior to that, even is the locus earliest in the pons, which projects nor epinephrine to many places, but including hippocampus and amygdala.

So really about, you know, it's about memory and it's about stress. And so many of these people, as you know, relatively early on will become somewhat passive and kind of be looking at the at the spouse to get answers and things like that, that kind of that.

They're not quite as engaged. And as they start to get better and it's one of the most common things I hear the spouse will say, wow, he or she is so much more engaged than they were before, just, you know, interacting with us better.

Yeah. And part of the art is, is to figure out, I think over time, these neuro modulatory approaches, you know, how they worked with, you know, cellular health.

And so, for example, what's what's really ideal about neurofeedback is it's very hard to do harm a patient because for the most part, they're training their own brain.

And we're giving them the information and how and how to do that. And we find that it it really does help to give the brain energy, you know, through maybe light or hyper barracks or other, you know, nutritional intervention.

And then the neurofeedback can oftentimes be a way in which the brain can kind of learn some of these network adjustments, you know, if you if you will.

But I think in isolation, I don't think it's nearly as helpful for cognitive improvement, even though there has been some evidence around that. And so one of the exciting things here is to figure out where are the synergies with different treatments.

Yeah, very, very interesting. Then I wanted to talk to you about one of your patients recently because it relates very much to an old story. So way back was this 40 years ago now when I was finishing up neurology at UCSF, a Nobel laureate came to UCSF specifically looking for a neurologist, a young neurologist who had just completed training.

So he spoke to several of us. And and a very interesting I ended up going and visiting this guy at his home and talking to him. It turned out that his wife had unfortunately developed developed cortical basal degeneration.

And at first they didn't know what the diagnosis was. This is a heart to some extent, as you know, Parkinson's like syndrome in some people. And but about 20% of these people or so will have Alzheimer's pathology, as it turns out.

And it's it was such an unusual presentation, and there's been very little on the genetics. Basically, it's there aren't that many something like 40,000 cases in the U. S.

And I thought he said something really interesting way back in the in the eighties. And he said, you know, the reason I'm interested in finding a neurologist who old trial he wanted someone to go and travel around the world and he said that the idea was he said since so little is known about this disease, how do we know that there isn't some simple explanation and some simple treatment that might actually help her?

You know, the doctors have told me him at the time that, you know, there's nothing that can be done. And indeed, she did progress and die, unfortunately.

And then you had a case recently where you were quite successful.

Using EEG and neurofeedback to guide treatment

And I know I wish you were still alive to talk with you about your case, because I think he would be intrigued about what you found. So maybe if you could tell us about your patient.

Sure. So this is a patient who came to us last year who was in her mid-fifties, a former Marine who served her country and had multiple tours of duty in in the Gulf, in Iraq, and really had had severe exposure to two toxicants.

A lot of the burn pits, a lot of the oil fires and and just significant, significant exposure. She had retired about 12 years ago. And, you know, one or two years after retirement started to have tremors and a left hand and migraines, which kind of progressed to word finding and aphasia.

And she had seen a functional medicine practitioner about three years before we saw her. And there was a number of dietary interventions that were done that really reduced the symptoms.

But the symptoms did recur and she was evaluated at at the VA and they did a amyloid PET scan that showed plaque in the temporal parietal and frontal areas that were just really unilateral, generalized volume loss in the in the right side.

And given the diagnosis of cortical basal degeneration and really told she had a few years to live and to really put her affairs in order. And so she came to us really from her, you know, functional medicine practitioner as a referral.

And when she came in, she really had pretty remarkable, you know, left arm rigidity. You know, my aloneness, you had a lot of them neglect and dystonia and a proxy and tremors sort of all on the left side.

And then her MOCA was 22 when we evaluated her. We she was happily three, three. We did do a neuro quant that basically showed that on the right side, almost everything was in the single digits in terms of volumes.

And a parietal was first percentile, occipital was first percentile, the temporal was fifth and general cortical gray was third. And then on the left side, everything was really normal.

While she did have a lot of innate immune system markers again that were elevated, the MMP nine was 1500. The C for I was 15,000. She had really bad dysbiosis on the GI effects and then on the vibrant toxin tests we did. You.

She basically had chemicals, moles and meadows. But the degree of elevation, you know, without being provoked was about 400 to 500% higher than the 90th percentile, just on a really large different amount of chemicals, including glyphosate and organic phosphates and heavy metals.

And so in her case, you know, resources were an issue and so we really tried to design a program that could try to be covered by insurance and could move very, very quickly.

And so we did really start her on a wild protocol type of nutritional intervention. But just to give you a sense, rather than nine cups of vegetables a day, she did.

And she was taking about 16, 17 cups of vegetables a day. Wow. In our sauna every other day, heavy exercise. I got into a very aggressive P. T. A. program at the VA.

We did find that she had sleep apnea and that wasn't being appropriately addressed. And we got that implementation. We did start our on high dose thiamin and estrogen and really just a modest amount of supplements.

Just we were very cautious about finances and just, you know, for supplements and addressing BNF and mitochondria and amyloid clearance. And it was very we were able to find a place that did donate hyperbaric for her service and she was able to get heart chamber hyperbaric at two atmospheres for our find the Israeli protocols for about 40 treatments and within four months her MOCA had improved from 22 to 28 and she had significant improvement of her hand function.

So to the degree that she could stack quarters and still have for now not regaining full function but you know, market improvement in a positive direction as opposed to just halting, you know, halting decline.

And importantly, there's hope, you know, is that, you know, she is she has she has hope that there are things that can be done and that the you know, we it was it was fortunate we were able to get hyperbaric but is also you don't need to have oftentimes the you know the aggressive interventions to to make a difference.

I think the main thing that you know, where there was very good response was the dietary, you know, protocol. So rather than using our supplements, we really did try to use diet to really accelerate detox and, you know, should be coming in in person this summer and we'll be able to see how much toxic and she's been able to clear.

Yeah. Wow. Fantastic.

Case study: cortical basal degeneration and multimodal recovery

And has she been pretty compliant with your overall approach? Well, I would say that her compliance is 110%. So it's just that there's there's been it's been it's been a pleasure, you know, in terms of designing and working together program that that she could do.

One of the things that's fascinating to me as a as a neurologist who's, you know, spent my whole career being told there's nothing you can do about any of these degenerative diseases.

You know, we've now seen at least an of one for ALS or Alzheimer's or familial Alzheimer's for Lewy body or cortical basal degeneration, you know, on and on and on.

ALS, we see, you know, again and again and again. We're seeing, of course, with Terri walls work wonderful results with MMS as well. So all these diseases that have been very difficult to treat, we're starting to see hope and we're starting to see, you know, real breakthroughs.

If you look at the right place, you can really see and for many of these people, what's driving the problem and you can really get at it and ultimately help these people.

So this is such exciting news because, you know, again, so many people are just told, as she was, that it's hopeless and get your affairs in order because things are only going to go in a single direction.

So congratulations. That is truly, truly exciting. I wanted to ask specifics about the hyperbaric because, you know, some people use this, some people don't.

I know you've used this extensively now with the Israeli group. They like the idea that you give some hyperbaric. And of course, they argue that it could only be hardshell, that it shouldn't be softshell.

And then they argued that you should have about 5 minutes where you do. It's, as they point out, relative hypoxia. You're not going below atmospheric, but you're bringing them back just for a few minutes.

And their argument was you get two different positive outcomes, one from the extra oxygen and the and the other one then from the secretion of trophic factors that occurs when you start to come back down.

So how do you do this when you do your treatments? Yes. So on the hyperbaric side, I think it's a that's a really good example of how interventions are sort of rapidly evolving.

So now when we first started to do this, I remember reviewing a evidence based review from that from the VA, where they basically devoted two or three pages sort of concluding that hyperbaric there's shamanistic ritual of putting patients and that in the chamber was really driving these results when really what was happening is there was a methodological issue of how to create the right placebo group.

And I do think that Dr. Fris Group should be congratulated on really getting the placebo group right because, you know, as you know, what they've done is they've put a number of patients into these a large multi chamber and then they pop the pressure up so that everybody thinks even in the placebo group that they're getting hyperbaric.

But then within 5 minutes they rapidly reduce the pressure and then they give patients rooms instead of oxygen. And because the placebo group is very strong, I think their methodology now is convincingly showing the difference.

Yeah. And what we've seen over time with Hyperbaric is if there is a lot of inflammation, especially with patients with a lot of muscle or potentially muscle related information or even COVID now related information, they can be very sensitive to pressure.

And so I would say in a number of patients that have come from know hyperbaric protocols where they're almost

sort of automatically put to two atmospheres and come with really, you know, adverse side effects.

And so what we'll do is we'll start low at 1.3 atmospheres if need be, and then kind of and move it up. And because the data moved in that direction, we initially were doing, you know, 1.3, 1.5 atmospheres.

We now have chambers that will go up to 2.2 atmospheres, but, you know, down to 1.2 or 1.3. So we'll get the pressure. That's right. For the patient. The you know, the the arguments that the Israelis make around the hypoxia and hypoxia phenomena makes sense.

Now, nobody has studied, you know, if you if you stay at that pressure and you and you compare one versus the other, it's not been randomized. But we we use that protocol because it's relatively straightforward to do.

We have a chamber that's not full of oxygen, but rather the patients are breathing 100% oxygen through a mask. And so it's easier for them to do the air brake.

But that's because our chambers are really designed for neurologic symptoms rather than generalized wound healing. So so but we have seen, you know, as in the first case, if sometimes patients can afford the hot, hard chamber and the soft chamber can be a relatively cost effective option.

But our advice is always to try to get that at 1.5 atmospheres, if you can, so that there can be some more flexibility. I do think there's a little bit more data around 1.5 atmospheres for neurologic than 1.3.

So yeah. Yeah. Very, very interesting. Okay. And have you begun to use any of the new blood tests yet? Things like phosphatase 181 and you know, pre 70 C two and that sort of thing.

Have you begun to use any of those as, as markers? Yeah. So, you know, we started, you know, hearing about that from from you over the of the fall. And so we've been starting to use those probably not enough yet to have a good sense, you know, of of the right use, certainly, you know, chronologically to to see.

But now, for example, where I think this could be very exciting is I think that when we look at how powerful autophagy can really be as an intervention, you know, I think we're very, very excited to look at some of those markers and see what happens if we really try to dial up the autophagy in a liver, potentially with more prolonged fasting and that and patients who can handle that.

You know, what would be the impact on some of these misfolded proteins? And I think that will really be, you know, become a standard of care as soon as we can get reliability from the labs that, you know, we kind of understand.

But, you know, the natural variability and the confidence intervals of the testing. Yeah, exactly. So, you know, one of the interesting things has come out of all this is we're all seeing now it's absolutely possible to make people better.

It's happening all the time. We're hearing all these wonderful stories, but making it more practical, simplifying it and making it less costly is, you know, a goal that we'd all like to see. We'd all like to see this that's completely reimbursable, it's easy to do, etc..

And I know you've taken some wonderful steps in that direction. Do you so do you work a lot with health coaches to help with this or not? Now we have we have a health coach as part of our practice, and I absolutely think that that using health coaches is going to be a critical way to lower lower the cost.

You know, as we know, I talk about some of what we do to a group of, you know, residents yearly. And, you know, one of the immediate feedback is, wow, this is really expensive.

And I'm like, well, how does that compare to monoclonal antibody centers like our monoclonal is are more expensive. But, you know, I'm confident that as we get to the, you know, proof of concept in some of these trials, that there is an ability to take half the cost out, if not more.

But it just has to be done, you know, step by step, you know, if you if you will. And and then the real key thing is to is, as we get to patients earlier and earlier, which is really the desired outcome, it will be cheaper and cheaper to be able to intervene, you know.

Hyperbaric oxygen, biomarkers, and cost-effective care

And so I think a good way of potentially doing this is now in is probably working with some of the physician groups that have more independence and making decision making.

So you see that certainly down here in South Florida, there are a number of physician groups that take full risk with Medicare that have more leeway in terms of making clinically guided, you know, benefit decisions.

And I think that you know, after the clinical trial, that could be a great way to start to, you know, get this covered by insurance, as, you know, make a deal to say, hey, for a fixed amount X.

Well, we'll get, you know, the the most cost effective set of, you know, interventions. But there's still a lot of work to do to dis, you know, to disaggregate what is, you know, what really makes a difference.

And now in my clinical experience that when when you intervene early, there's, you know, you can really get to a pretty cost effective intervention. But if you're coming late, it's it's it's definitely going to elevate the, you know, the cost to intervene, which makes sense in general with disease.

So absolutely. And so common chronic illness. And, of course, people don't, as you pointed out, they don't think about the cost of the monoclonal antibodies because they think, well, Medicare is going to cover that. Right.

And of course, the pharmaceutical companies will do everything in their power to lean on the Medicare services. You know, the recent claim from the head of Lilly was, you know, we're going to get this covered, you know, one way or the other.

We think they'll do it wink, wink. So we need to find ways for them to cover things that are actually much more effective and much less expensive and the same story, of course, with nursing homes.

And so, you know, my argument has been that all these policies that were sold on long term care, you know, this should be used instead of just watching people going into nursing homes and dying.

There's so much more that can be done ahead of time to keep them out and to keep them doing very, very well. Well, I think one of the expected I think one of the the the new forces that's going to, I think, change the dialog is the impact of COVID on cognitive function.

So I think in COVID, we're both saying that, you know, older patients are, you know, when there's a sudden decline, you know, COVID and that and the top three less step up being the, you know, the cause of a sudden decline in cognition.

But there is an increasing number of people in their thirties and forties or even twenties who are having cognitive impairment as a result of COVID and its attendant complications and and that and when, when you just think about that purely from a economist's perspective that the you know, getting multimodal interventions right is, is going to be the way out of this.

I don't suspect there's going to be a easy sort of, you know, single shot approach to helping people out of this. It's going to be the same principles that that are being done for for older adults will apply absolutely.

To younger adults. And the same abnormalities we're seeing in the innate immune system there, there's an overlap. But, you know, there there's certainly overlap in common mechanism and that can be solved through the approach that you start first started to articulate a decade ago.

Yeah, it's a good point. And you know, I wanted to mention quickly because you mentioned Mast cells earlier on in our conversation and we had, as I mentioned before, we to you, you know, we had an amazing case where someone has mass Marcell mass cell activation disorder and it had cognitive decline and just had a striking response, interestingly, to Nurtec to an anti CG r.p.

Yeah, I know you've tried Uber. LV And have you had similar results with any of your patients? Yeah. So there's no question that the CG ARP antagonists are are helpful in that they're younger patients.

So I certainly seen with a lot of patients with, with COVID and other sort of clear inflammatory conditions that a trial of nurtec or Brown V you can see results as soon as and 2 to 3 days.

And if that's the case, you know then then the issue is is trying to get the coverage to to happen to to see that improvement. I've not yet seen it on, let's say, somebody who's and they're in their seventies with cognitive impairment, but we are starting to test that and seeing what we can do.

Yeah, I think it's interesting because you know, it just shows that of the many contributors that we can all see, that's one that we shouldn't miss and certainly is one that may be active.

And I of course, I don't know what's going to turn out to be point 1% of the patients or 50% of the patients. But certainly seeing the one who that responded so well made me sit up and take notice that, okay, let's let's not miss that particular so. And also where the COVID intersection happens.

Another good example is just with the, you know, natto kinase. So you're kind of clearly seeing that it has a benefit in long COVID, that it has cellular activity against spike protein in the lab.

But as we went into a deeper and I had not known this, you know, a year ago, that that there's some very compelling cohort data and from China and it's not randomized but it is very good sort of year or two data that shows that when you are at high dose natto kinase, so above 10,000 nephews, you're able to decrease both coronary and carotid plaque by 30%.

And so that signal to noise ratio is tremendous. You know, statins, high dose statins are only in the single digit range. And so if you have had an intervention that is very safe, that's actually able to improve that, you know, vascular flow and reduce plaque, that's going to be tremendous and our whole set of interventions.

So and you've not had any problem with bleeding complications with that? We have not had any major bleeding complications with using natto kinase or lumbar kinase.

I mean, we're always sort of careful to start the dose low and then to kind of go up slope and but not seen any major problem whatsoever compared to, let's say, like using, you know, Eliquis or something that's in our pharmaceutical that's that's going after the same pathway.

Wow. Very, very interesting. Okay. Thanks, Greg. And then finally, could you talk a little bit about the upcoming trial? Of course, you are one of six sites, Hollywood, Florida, along with Nashville and Cleveland and Sacramento and Oakland and San Francisco.

And and we would love to hear more about what's the plan for the upcoming trial. Well, the plan for the upcoming trial is we are actively looking for patients and excited to enroll patients in the trial that the major required ment is going to be, that there is cognitive impairment, and that you do live within an hour's drive of Hollywood, Florida and, you know, probably the you know, the biggest concern we have about this is the patients who might be in the group that's getting the intervention.

Nine months later. You know, that's yeah, we're certainly asking them to wait, but that's happened in multiple other trials around around lifestyle based interventions and with the team that we've put together on site is going to be the team that's implementing this.

And you know, we've been very excited to to get this going and feel like this is critical to kind of show the research community that there is a strong signal from these interventions and that it holds up when we look at it compared to a control.

Clinical trial plans and lessons from responders and nonresponders

And then really the right step is going to be now there's always can be criticism of any trial, but if we show just the same level of improvement that we did in the proof of concept trial, I think it's going to make a very strong argument that we just need to do more research into these areas and get very, you know, precise about it.

When you think about the overall, you know, billions of dollars that have gone into just, you know, anti amyloid interventions. And if you can just take 10%, 20% and move it into some of these type of interventions, I think it would move the field, you know, very, very rapidly.

Absolutely. And then finally, could you tell us a little maybe one thing that you have learned from Pete, from people who who continue to decline, that that didn't do well.

And one thing you learned from someone who did well. So I think that from people who continue to decline, I think that there are definitely a set of things that when we've gone back and looked at and we have done this, we looked at all of our patients and said, you know, who didn't improve as much as we wanted, you know, what did they have in common?

And there are a couple of characteristics. You know, I think one was absolutely having a large amount of atrophy, so defined as really having, you know, the neuro quant might be a know half of the neuro quant is is a sea of red, meaning that it's, you know, less than a fifth percentile in terms of size.

You know, that's that's clearly a hard prognostic factor to overcome. I think the other other one can be the environment. You know, if somebody is in an environment and clearly in South Florida, mold is a very big challenge.

You know, we're just getting into hurricane season and another month. And and so when there's a constant exposure that can certainly be a negative prognostic factor.

And I think the and and I think that hope is the other one, where if we ask a lot of people in terms of changing their their their lifestyle and making those changes, you know, people need to see that that's going to make a difference.

And so, you know, kind of getting to that threshold, the fact in the first six months, if you if you don't get to that, that, you know, sometimes people do lose hope.

And so, you know, we've kind of taken some of those lessons learned and and and moved it and to and to others and to our and to our protocols. And I think the other piece is that, you know, there's certainly been numerous occasions where we haven't been able to make as much progress.

And then we reach out to a colleague or two and get a and new insight on something that does make a difference. And, you know, I think we're all in this together as a community.

You know, there should be nothing proprietary here. It's all about just basically sharing and getting to, you know, create more effective programs every day.

And I'm more than happy to collaborate with anybody on this. Fantastic. Well, Dr. Craig TARDIO, thank you so much. This is fantastic. Congratulations on all the great outcomes.

I'm so excited to have you involved with this trial and look forward to more and continuing great results. So thanks so much for your wisdom and your experience and your input.

Thank you very much, Dale. And just I really wanted to, you know, let you know how much I appreciate your leadership and all the work that you have done in this area and pioneered you, I think, are really leaving a unbelievably unbelievable legacy.

So thank you. Well, I'm hoping we're going to keep pushing this forward. All of us together. So thanks again for all the great work. All right. Thanks. Take care.

Bye bye. Bye.