Hope For Hard-To-Treat Babesia: Inside The Tafenoquine Clinical Trials Transcript

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Introduction and Guest Background

Hello everyone. My name is Doctor Richard Horowitz and I am the co-host of the Doctor Talk Killing Lyme Summit 2.0. It is my great pleasure today to introduce you, Jeff Zhao, who is heading up 60 degrees Pharmaceutical.

And we're going to discuss today BCA and our coda to Phoenix for the treatment of the BCA. With the new clinical trial that's going on and some of the prior history of using it for malaria prevention.

So, Jeff, I really appreciate your getting on today because the BCA is a really big problem in my practice, and I know in a lot of the Lyme patients world, we're seeing it all the time.

So thank you for joining us. Oh no worries doctor. It's it's really great to be with you here today. And I hopefully I can shed some light on all things Stefanik Khan and, in various aspects.

Yeah. So so tell people, how exactly did you get into the science world and, kind of head up six degrees pharmaceutical. What's your background and how did you get into this?

So, my family's in the mining industry originally, so I traveled around a lot as a kid, including to some places, tropical places with a lot of, income in income and health inequality.

And, that sort of exposed me to global diseases a little bit. And so as a, as a science student and eventually a PhD candidate, I became interested in malaria and drug discovery.

And when I was finished with grad school in Australia, that led me to a, Walter Reed Army Institute of Research in Washington, DC, where I worked on, to fan action for malaria in various aspects.

Before founding 60 Degrees Pharma in about 2010. So like almost 15 years ago. Well, you know, your timing was great because I think a lot of people know my story.

But I was the first doctor to diagnose babesiosis in the Hudson Valley, New York. I'm going back into the 1990s. And, the case that led this to me was this woman in a wheelchair who was she couldn't walk for five years, basically paralyzed for the waist down.

And had these drenching sweats, in her 30s. And we had done a differential diagnosis. And, you know, we ruled out malaria, hypothyroidism, non-Hodgkin's lymphoma, tuberculosis, autoimmune.

We went through everything, and we were not supposed to have Busia in our area. So we ultimately took her blood. We sent out the ticks from our area in the Hudson Valley.

We found, in fact, that a few percentage of them did have the Busia. She ended up being positive by PCR in the blood for the Busia micro. We at the time met his death from a total con and his death through mice and worked.

These were the good old days when the drugs for you know, this disease worked and lo and behold, within the weeks, two months later, she walked out on the wheelchair.

I mean, the woman is skiing at this point and it was primarily treating the Busia right. So I, I got an early on kind of take of like how important this parasite is that, you know, it's not just giving you day sweats and night sweats and chills and making you tired.

I mean, this thing can destroy people's lives. This woman was so sick, she couldn't even get out of a wheelchair. So years ago, the drugs worked. I, we, I had published, you know, even abstracts on mefloquine.

Right. The precursor to to Phoenix and years ago, because I was finding clindamycin and quinine and a terrible con is that for mice and stop working and this goes back even 20 years ago.

Babesiosis in Clinical Practice

So I'm really happy that you started working on this around 2010, because, boy, there's a big need in the clinical space, for drugs that hit these malarial type parasites.

Particularly in patients who have longstanding infections that, you know, aren't responsive to other things. You know, in the anecdotal interactions we have with physicians and patients, we hear about that all the time. So, we're doing what we can to help.

Yes. And and, you know, with malaria being I don't think people realize, like, how severe malaria is in the world. I know they've tried to develop vaccines, which have had some, efficacy.

Still not great. But I mean, there's like millions and millions of people that still die, right, every year from malaria. So, you know, to create a drug that's effective for malaria prevention.

You know, when I went to India years ago, I'm pretty sure, in fact, I was taking them a flow queen once a week or something because I've gone to India many times.

Right. And in Thailand and other places. So, so how did the. So I understand that you're in these other countries, you were seeing the need and how did it come about that this drug discovery actually happened?

Yeah. So the I mean, coming out of the Korean War, had successfully gotten prime equipment, which was the original 80 minute Queensland precursor to panic when approved for the radical cure of vivax malaria.

And vivax malaria has a quiescent liver stage which reactivates and causes relapse. And 80 minute Queensland's like prime. It went into panic when a uniquely active against that particular stage of the parasite.

The problem with private coin is its half life is only six hours. And unless you take it religiously as prescribed by the CDC, then if you're exposed to malaria, you will contract it.

And so what the Army was trying to do was develop a long, half life version of, prime Aquaman. And they started in 1978. And then by the time 60 degrees was in a position to license the Army's data and began a public private partnership with them over several years.

You know, it had been almost 30 years or 35 years, in development before, our involvement in that project. So we partnered with them in 2015. And then, our role was to complete a couple of clinical trials, put the dossier together with a lot of help from other partners, and we were successful in getting to get approved for weekly prophylaxis of malaria for up to six months in 2018.

And that was the original, indication and commercial purpose for developing. Anyone got it. So, so if someone like myself who I haven't traveled in a while, Covid kind of put a kibosh on it.

But, in the past I've been to Thailand, I've been to India, I've traveled a lot in malaria places, and, you know, they would talk about doxy cycling prophylactically or malaria control, or, you know, mefloquine.

So, this is now pretty much standard of care. Like, if I was now going to go to India or Thailand or a place where it has malaria, the dosage this would be basically I would be taking to, basically once a week.

Yeah. So the the approved diet for malaria prevention is a weekly, sorry a loading dose over three days, 200mg a day for three days and then 200mg once a week during travel, for up to six months and then, subsequently.

We've also, generated safety data that have proven out the safety profile for up to a year. Eric Hyder offers a

couple of benefits over the the alternative medications you mentioned.

One is once weekly, which is really nice for patients who, have trouble remembering to take their medications. I'm one of those folks, so I certainly, appreciate the option of a once weekly regimen.

And then the other advantage is when you get back, you don't have to do any post-exposure prophylaxis apart from one dose. And that's because of the two week half life of tiffin equipment and the fact that it kills those, quiescent liver stages that I was talking about.

As far as we know, unlike with mefloquine, and at a time when there's no drug resistance been reported, really for Atum and equivalents in general. And, so that's another benefit that Eric of has for malaria prevention.

And the mechanism of action from what I've understood it's, it's oxidative stress against the parasite. Is that one of the major mechanisms of how it's working.

Yeah. That seems to be the pre, the non-clinical work that's been published seems to indicate an activation to oxidative intermediates, intracellular Lee.

Origins of Tafenoquine and Malaria Prevention

And then that generates hydrogen peroxide radicals which kill off parasites in very specific locations. So in the liver, in the blood, in the red blood cells, and in the bone marrow for the give me the sites of Plasmodium falciparum.

Right. And, you know, regarding that, I mean, that's been I think one of the big questions for Lyme patients for years because, I would say on the average it's at least 80% of my patients who have the BSE.

I mean, it's higher in the studies I have published in the literature, it's varied somewhere between 60 and 80. But I can tell you over time it's at some point it's almost everybody who comes into my practice who's chronically ill, who has it.

Do we know, just like malaria, when it has the phase in the liver that it hides and bone marrow, do we know exactly where this parasite is hiding? Because there's there's been theories about it, but I've never seen anything that's been absolutely like, convinced me as to where it's hiding and why it's relapsing.

Well, I don't know where it's hiding. And, I've read I've read a few papers and I've talked to other people who, much smarter than me on the on the basic biology of Bayesian.

I'm in these long term infections. I don't think there's much in the scientific literature about, you know, is there a quiescent stage, the way that there is recognized for Plasmodium vivax malaria and and even Plasmodium malaria, which, you know, recrudescence from a quiescent blood stage parasite, the the biology seems to be much more advanced and understood for malaria than it is for the diseases and how the busy Osis infections reactivate.

Right? Although although we know like the Red cross, when when people give blood in Connecticut, they know that they're finding, right. They will find a Bayesian microbe in the blood of people who are pretty much asymptomatic. Right?

They have to screen them very carefully. Right. But yes. In some of those, some of those DNA positive cases can last for, you know, a year or more. And you're that's beyond the point where red blood cells, you know, the half life of a red blood cell is 120 days.

So what is happening after day one? 20 in patients with, PCR positive, infection, but but no symptoms. Yeah. And I don't know the answer to that. Yeah.

Because we, we see recrudescence all the time in our patients. We have patients. For example, I will treat them with, nine weeks of dapt, some combination therapy for Lyme.

And the is quiescent. Just had a patient like this. And they'll be okay actually for a couple of months. And all of a sudden they'll start getting symptoms and we'll get a bbca fish that's positive.

And it's not the first time we've seen this, that sometimes we knock down the look of certain infections and and it comes out. But, it's clearly a big problem.

And for those of you who are listening, I'm speaking with Jeff Dow from 60 Degrees Farmer. We're talking about our coda to and, which we're going to talk about the clinical trial that's ongoing now for.

But I think you're just in fact, I saw it in the literature. You just signed up the first patient, I think just was it a couple of weeks ago? It. Yeah.

So, you know, one of the nice things that's, happened over the last few years is there's been a lot of basic research done with, to farm equipment in, various animal models.

And those non-clinical studies seem to suggest that Tiffany corn is active against various kinds of the busier parasites in both, animals with normal immune systems and animals with compromised immune systems.

And if, the the drug is given for long enough in those animal models, it confers a sterile protection. Now, animal models on humans and, and every scientists will tell you that you can't predict human disease based on mice.

But the good news is that there are some, cases beginning to come out, and in particular, the one from Yale that was published in June of last year, which showed in five immunosuppressed patients given, to Faneca, one with a lightning dose, and then once a week for at least six weeks, in combination with standard of care medications led to cure.

And 80% of patients who had previously failed multiple rounds of standard of care medications. So yeah, anecdotal studies like that are obviously a bias because of the publication bias towards positive results and data, but they are suggestive of a potential role that Quinn might play.

And so our clinical program is really designed to replicate those findings and provide the data, to hopefully go to FDA and seek some label modifications to allow it to be prescribed, in various kinds of BBC ISIS.

How Tafenoquine Works and Babesiosis Biology

So we have actually three clinical trials that are either ongoing or planned. So one of them is a study in severe versus amongst hospitalized patients.

So that's a randomized study that we're doing it. Yale. Right. Island hospital, one of the Harvard sites and, Tufts and we've enrolled six patients out of a target, 33.

And we expect to be finished with that study by the end of, the 2025 tick season. The study you mentioned is a open label study, under an expanded access route, for patients who are immunosuppressed and have failed prior medications.

And we're providing the, to fanatic plan on a compassionate use basis and then collecting some data to support, hopefully, hopefully that future, FDA interaction.

And then this study we're working on in the planning phases for at the moment is a, a study in chronic diseases, where there's clinical symptoms of ISIS as some laboratory evidence of infection. And, and that's designed to try and collect evidence and data to reflect the patient experience that, you know, perhaps some of your patients are more familiar with and, again, so that we can kind of, standardize the, the information and provide that to, physicians and the regulatory agencies.

Yeah. Well, you know, Tom Moorcroft and I did, we did a talk that will be aired, actually shortly about to the clinic

about different but easier treatments.

And, you know, we're both finding and again, we're not to back at FDA when we talk about your company, I'm talking about my personal experience and Tom's is that it's at least an 80% success rate.

Because we can't really use any of the older drugs anymore. They really, really just don't work in our patients now, you know, our our patients are immunocompromised.

The answer is yes. Some of them are, Lyman Bartonella patients. A lot of them do have, a problem with immuno compromised. Their immuno globulin levels are low, their subclasses are low.

Some have had long Covid. They have T-cell exhaustion. So in a sense, a lot of our patients are immunocompromised. And we have used, the loading dose of 2 to 200 a day, three days in a row, once a week for six weeks.

Not standardized the way you've done it. But, some patients I may have given Mallon with it, some a terrible concept from X, because we didn't know early on how effective.

But I can tell you that, in my experience in Tom's, we have not published this this is just we're talking about our clinical experience. Now, it's at least an 80% success rate, probably higher that that we're seeing at this point.

And what I really liked about it is we're not really seeing a lot of the side effects. You know, when I do DApps on one of the major side effects, if that zone is, elevated hemoglobin levels where you don't carry oxygen well, in the blood, and you get anemia with, you know, hemolysis.

And I've been able to minimize that somewhat very high dose folic acid to block that effect with dapt shown using methylene blue. The nice part is, is that, you know, when I follow my hemagglutinin levels and I follow counts, I might see a little bit of anemia, I might see a little bit of hemoglobin, but people seem to tolerate it extremely well.

So, for me at least, it's very promising. And it's important because it's not just from a tick bite. I published a case, several years ago of a woman from Europe who had four pregnancies in a row, and two of them.

She reactivated her boobs busy in the third trimester. The child could have had hemolysis with jaundice at birth. At that point, we gave her clindamycin.

The concept Max and the the children were fine, but, you know, it's a big problem because you're getting it in the blood supply. You're getting it from maternal fetal transmission and even, organ transplantation.

So people can get the BCA from many different sources. Now, using it in pregnancy. It's at this point it's not a drug that can be used in pregnancy. Is that correct?

Yeah. It's a fan of Quinn is contraindicated in pregnancy. And the reason for that is there isn't any way of testing the G6 status of other fetus. Yeah.

So even though it's, not a likely, well, I can't really comment on whether it's a likely or not a likely risk.

Clinical Trials and Expanded Access for Babesiosis

It's just the fact that it's extremely difficult to obtain a fetal blood sample and therefore definitively know that someone doesn't have G6 be the deficiency, and there's no way to predict it based on the, g6 g6 piece g6 pd status of the mother or the father.

So that's the main reason for the contraindication in pregnancy. If it's a fan of Quinn and Prime Quinn. Right. And I hope you do. I hope you do publish your, experience with Tiffany Quinn in chronic disease, because, you know, people need to hear that.

And it's so much easier to have a conversation about things more broadly when something's, you know, in the medical literature and, and gone through all the hoops.

So, yeah, I encourage you to get that out there. If you can't, no, I will. I promised my wife because I've pretty much been publishing every year and I'm starting to, you know, just pull back a little bit.

I in fact, we just submitted last week, for an NIH grant for a planning phase in our 34 planning grace for a, randomized, multicenter, placebo controlled Epsom trial for the treatment of chronic Lyme LDS.

So that just got submitted last week. And I can tell you and and God bless you for doing these trials. I had no idea what it was like trying to get NIH grants, like what you have to go through just to be able to submit and get these trials done.

So, so I was in the midst of that, but I will look at the data this year. I may have a little bit of time. I'm working on a book right now for, for Simon and Schuster.

And get a whole series of people who have who have taken, and recorded to Fennec Quinn at this point, the difference will be, of course, with our series, as we weren't sure I needed to make sure the patients got better.

So a lot of times we were mixing it with a chocolate cone. And is that for mice and or Mallon? I may have some patients who've taken it alone, but, odds are, I think in the way we did it.

Because I just wanted it to be a home run out of the park. I didn't want to take a chance. A lot of these people were taking, artemisinin, which, again, with malaria, it's now become resistant.

But they were also doing, like Chinese skullcap, Japanese knotweed, a cornea. They were doing other types of, herbs that have been shown to be effective in, like for example, the PCR done.

Can I so we, we will kind of do in the kitchen sink approach knowing it was safe. And that is scientific. Like we don't have randomized trials. But I can tell you nevertheless, patients who had failed a lot of the prior protocols who are fish positive, RNA positive in the blood, who I could not get rid of it.

We have definitely had some successes using it. And I will try and get that published. As long as my wife gives me permission to go through the data, you probably know at some point you've got to get your wife's permission after 30 years of marriage to, to get some of this stuff out there, but I. Yes, I will definitely look at it.

I think you'll learn what your responsibilities are. Easily the older you get on that front. And congratulations on getting the NIH grant submitted. It's.

Yeah. You know, it's just a. Shame that. It takes a long time. By the way, we don't hear back for, like, a year. And then we have to get the statistician.

I mean, it's a very long process. So I don't think people realize like the the trials you're doing right now. It's a lot of legwork to be able to get this done.

And I really applaud you and your company for doing it. And at least from my experience, I think you're going to have a home run, I think from at least a preliminary data, not speaking from FDA or anything else.

My personal experience, I do think you're going to have a, a home run on your hand. Based on what I've been saying. Well, thanks for the encouragement.

And, we'll, we'll see how the trials go. And, you know, hopefully we get a receptive regulator at the end. If, the trends we hope to see pan out. Yes. So, if people want to find out more about the trials, you said they're one of them is open label.

If people want to find out more about it or get more information on to Fenech, Quinn and you and what you're doing. How do they contact you? Where do they get that information from at this point.

So we have a link on our website. So it's, you know, 60 degrees Famicom. There's a clinical pipeline tab, and then there's a, a button to to click, which will give you more information on the clinical trial program for the PCOS.

You know, many companies have inquired at our inquiries. Line is inquiries at 60 degrees Famicom and, every company has one of those. But we actually answer the emails relatively, responsively.

And then, I'm obligated to share that, on our product website, which is our code A.com. There is obviously the important safety information for prescribing for malaria, but also contact numbers if you need to call, about adverse events or, you know, medical issues related to the product.

That's great. That's great. No, I think look at it. It's a very important, medication you've been working on. I didn't realize you've been working on this since 2010, and it came out of the Army research.

I think it's fabulous when you get these, private public partnerships that, you know, are going on this way. I think it's fabulous. So, any other information you think that people should know about our code as far as, the trial side effects, efficacy, any anything else you think would be important to share with the public?

So, you know, we've been to a number of conferences focused on tick borne disease and what we we sort of emphasize two things. One is the clinical trial program and our commitment to generating, data to validate patient experience and inform, you know, the regulatory process.

Safety, Side Effects, and Pregnancy Considerations

I think the other thing is just highlighting the importance of, getting the most relevant and up to date safety information. And there are two places you can get that, one is that the product website, Erica.

Mediacom. And, that's the synthesis of the FDA's advice related to, safety in the context of malaria prevention. And then the other, important place is a publication that we put out in 2022, in travel medicine and infectious disease.

It's by Navot Moreno et al. And that documents the it's a double blind, randomized, placebo controlled trial comparing weekly to Phoenix and following a lighting dose to placebo for 12 months continuous dosing.

And we looked at ophthalmologists safety, psychiatric safety, as well as did a lot of routine clinical chem, CDC and the routine adverse event reporting at regular intervals throughout the study.

And, you know, overall, it reinforced the nine, drug related adverse events that, you know, have been described for a minute, quit one such as, you know, a small increase in hemoglobin anemia that resolves, small change, small predictable changes in or decreases in hemoglobin that resolve over time.

And these are folks have been screened for G6BD deficiency. And that helped to dispel some of the myths about, psychiatric risks associated with Quinlan anti-malaria because we did baseline psychiatric exams and followed various psychiatric inventories throughout the study.

And they suggest that, in the context we use where the label was followed, the risk of psychiatric adverse events was no more than placebo, even in patients with prior medical history.

Provided the labels followed the way it's supposed to be. Right? And for those who don't, you know, the history of drug development with malaria. But the reason this was coming out is because mefloquine Liam, which, by the way, I've used easily, I'm not exaggerating the numbers.

Over a thousand, a thousand doses easily, 1000 patient experiences over 30 something years, because that was, you know, very long, half life. But the difference is it was affecting the interval.

I had to make sure people for acute drugs, but there was a black box warning because I guess vets came back, you know, years ago with psychiatric trauma, took this, with the load learned over time when I had to kind of play around with these drugs years ago when I was searching for answers for Bbca, that we did not find that we ended up seeing those kind of psychiatric side effects.

And eventually, of course, they took off the label, but that's of course, why you had to do that is because it was like a cousin of one of the drugs that was out there, in the past.

But yes, I agree, I it seems to be, at least from our experience, extremely well tolerated. Again, personal experience, not your company's experience.

Where to Learn More and Closing Remarks

We've really not seen any problems with it. And and in our patients, they're very complicated because my patients are not straight bbca. My my patients are Lyme and Bartonella that do have psychiatric issues.

And we we have not seen it. It seems to be very well tolerated in our patient population. So again, I think I wish you well in this. I think, thank God you've been doing the work on this.

And I think you're going to find that it's going to be quite effective when you get the final results of the clinical trial. And, and I will speak to my wife about going through those case studies to see if I can get a few of them in the medical literature.

Yeah, I'm looking forward to reading that paper. And, and, seeing you at the next conference. I appreciate it. So, thank you again for joining us today, Jeff.

That was it was a real pleasure speaking to you and letting people know about our cognitive decline. And, some of the trials you're doing for Rebecca.

So for those, again, who've been tuning in, my name is Doctor Richard Horowitz. I'm the co-host of The Doctor Talk Killing Time Summit 2.0. We've been speaking to Jeff Dow from Six Degrees Pharmaceutical.

Really about an important topic, but BCA and some of the treatments that we're looking at right now to help a lot of our suffering patients who have this malarial type parasite.

So thank you again for joining us. And I look forward to seeing everyone soon in the near future. Thank you.