LEUKEMIA & LYMPHOMA SOCIETY®

THE BLOODLINE WITH LLS

A PODCAST FOR PATIENTS AND CAREGIVERS

Episode: 'Advancing the Science: Chronic Myelomonocytic Leukemia (CMML)'

Description:

Chronic myelomonocytic leukemia (CMML) has been a challenging disease to tackle, historically treated with therapies meant for other conditions. But there's a new wave of hope!

Join us as Dr. Eric Padron of Moffitt Cancer Center and Dr. Lee Greenberger of The Leukemia & Lymphoma Society unveil the groundbreaking new CMML Initiative, fueled by recent funding aimed at revolutionizing treatment. Discover how this initiative is paving the way for individualized therapies that promise to enhance the quality of life for CMML patients and bring us closer to a cure.

Transcript:

Elissa: Welcome to *The Bloodline with LLS*. I'm Elissa. Thank you so much for joining us on this episode.

Today, we will be speaking with Dr. Eric Padron and Dr. Lee Greenberger about an exciting new initiative to advance treatments for chronic myelomonocytic leukemia, or CMML. Dr. Eric Padron is the Scientific Director of Malignant Hematology at Moffitt Cancer Center in Tampa, Florida, and Associate Professor of Medicine at the University of South Florida. His lab primarily investigates different approaches to treating patients with leukemia, focusing on CMML. Dr. Padron's clinical interests are the care and treatment of patients with adult myeloid malignancies, including myelodysplastic syndromes, or MDS, acute myeloid leukemia, or AML, and myeloproliferative neoplasms, or MPNs.

Dr. Greenberger is the Senior Vice President and Chief Scientific Officer of The Leukemia & Lymphoma Society. His responsibilities focus on planning and executing the strategy for all LLS research programs, including the CMML initiative. Dr. Greenberger guides LLS's mission to translate innovative research that ultimately will pave the way for new therapies to treat blood cancers.

Welcome, Dr. Padron and welcome back, Dr. Greenberger.

Lee Greenberger, PhD: Thank you.

Eric Padron, MD: Thank you. Glad to be here.

Elissa: So, our episode today is on chronic myelomonocytic leukemia, or CMML. Could you tell our listeners what that is and how it is different from other leukemias?

Dr. Padron: Sure. I'll start by saying how it's similar to other leukemias. So, like every leukemia, in fact, every cancer, CMML starts in the bone marrow, which is the place where we make all of our blood. It's the factory where all of our blood is made. And like any other cancer, it starts, we think, because the cells within the bone marrow acquire genetic changes that reprogram them to no longer listen to its body's cues and instead do its own thing.

We can talk more about how these mutations arise, but ultimately its own thing for CMML is, number one, ineffective production of blood. So, some patients are anemic. Some patients have low platelet counts. And then, number two, an elevation of a type of white blood cell called the monocyte, which is really the hallmark. You need that for the diagnosis of CMML. And that has its own clinical manifestations. People can have big spleens. They can itch really bad. They can have bone pain, joint pain, weight loss, things like that. So, it makes it unique from other leukemias. It is that it has features of both ineffective blood production and too much of a white blood cell monocyte.

Elissa: So, we know that CMML has some characteristics that put it under the umbrella of myelodysplastic syndromes, or MDS, and myeloproliferative neoplasms, or MPNs. What are those characteristics, and does it make it more difficult for patients to get an accurate CMML diagnosis versus getting diagnosed with MDS or a classic MPN?

Dr. Padron: It's a great question. I'll start by talking about what makes this what we call overlap syndromes; and that's what I alluded to earlier, the fact that there are both features of the disease in which the bone marrow, the factory cannot make enough blood cells and features of the bone marrow making too many of a white blood cell type. That collectively makes it an overlap syndrome.

Now, when it comes to the accurate diagnosis, there are a couple of challenges. So, one is a historical one. So, 15, 20 years ago, CMML, even if it was accurately identified, was actually a subtype of MDS in the World Health Organization (WHO) classification system. So, 20 years ago, if a patient had CMML, it would still be correct to say they have MDS. And that has led to things that have pros and cons; and that includes, number one, that oftentimes clinical trials for CMML are bunched in with MDS because of this historical classification. And two, when pathologists are diagnosing these cases, the historic classification of MDS makes it challenging, especially those that aren't focused on myeloid malignancies.

In terms of getting the correct diagnosis in 2024, it really is like a lot of rare cancers. If you think about it, you can diagnose it. So, it isn't like there's this incredible subjectivity that you have to have an expert pathologist look at it; although that would be ideal. It's more that the physician, the pathologist have to think, let me look at the monocyte count. Let me see how the monocyte subsets look because CMML is not just an increase of monocytes. It's an increase of a certain type of monocytes. And the tests to determine that are all available; and so, the biggest barrier – again, like any rare cancer – is thinking of it.

Elissa: So, regarding getting an accurate diagnosis, as we look into getting more treatments and potentially maybe targeted treatments, having a really accurate diagnosis of CMML is good, correct?

Dr. Padron: Yeah. Sometimes, the treatments for CMML and MDS are similar. So, a practical clinician may say, "Okay, you have MDS/CMML or you have MDS, but it doesn't change how I'll manage you today in certain aspects." And that is true. But when there does become a drug that's specific for CMML, then I think that'll help change the paradigm of how even the most practical clinicians look at this. So, there is interplay between both getting new drugs and having the right diagnosis, in my view.

Elissa: Are there different levels of severity of CMML, and could you tell us about the different subtypes?

Dr. Padron: Sure, absolutely. Like every cancer, the more we learn about it, the more we realize it's not just one disease entity. There are different subtypes.

There's a lot of ways that researchers, like myself, have tried to help categorize these diseases. One is adopted by the World Health Organization, which is based on the percentage of immature cells that they have in the bone marrow. These cells are called myeloblasts.

So, when those cells are less than 5%, that's the normal range. We call that CMML-1. When they get above 10% in the bone marrow, we call that CMML-2. And patients with CMML-2 generally have a more aggressive disease. It generally mimics more acute leukemias and MDS, so that's one way to classify.

We actually are doing research now to come up with a consensus model that the entire community agrees upon so that we can use it and standardize it.

Elissa: Okay. You mentioned being similar to acute leukemias. So, why do some patients, but not all, transition to acute myeloid leukemia, or AML? And is there a way to predict early on whether it will turn into AML?

Dr. Padron: So, that is a great question and a large focus in our lab is to understand that. And I'll tell you why. It's because when CMML patients come to see me in clinic, most of the time they've already seen an oncologist and perhaps have had treatment. Many of them are clinically asymptomatic; either they feel completely fine, or they have minor symptoms, maybe a little itching after a shower. And I generally quote about 70% of patients initially present that way.

Elissa: Wow.

Dr. Padron: And so, if we could keep patients just like that, I can tell you all of my patients say they'd be very happy. They can still work. They can do whatever they enjoy, even though the disease may still be there.

So, a big area in our research is trying to figure out exactly that. What are the factors that lead to this progression event? Whether that progression event is an acute leukemia, whether it's your symptoms getting worse, whether it's the white blood cell count increasing, we don't know yet.

We have a study now that's funded by the NIH (National Institutes of Health) and, in part, by [The] Leukemia & Lymphoma Society where we're following patients prospectively who are clinically asymptomatic; and we're calling them every month and asking them how they're doing. We're particularly interested in acute inflammatory events, so things like surgery, exacerbation of autoimmune diseases, bad infections, things like that because anecdotally we've seen that there does appear to be an interesting connection between the number of these acute inflammatory events and whether patients progress. We're doing a study to see statistically, if that's actually true; and if so, that may give us opportunities to mitigate that.

Elissa: Oh, wow. So, how does CMML actually develop? Is that coming from genetic mutations? And are there still things that researchers are really needing to learn about CMML?

Dr. Padron: Yeah, there's so many things that we're needing to learn about CMML. That's for sure.

What I would say though is that how CMML develops, at least our understanding of how it develops, is probably very similar to how other myeloid diseases develop, like MDS, like MPNs. And that is at some point our bodies acquire these genetic changes in the bone marrow, and it turns out that while they begin to be visible with modern testing in our 70s and 80s, that they're probably there many, many decades before that. And so, once these genetic changes start to pop up, it's sort of the combination of the genetic change and just the wrong environmental or external impact that we just haven't understood yet that ultimately leads to the disease developing.

Because we know that in patients who have these genetic changes and don't have blood problems, these patients are called patients with clonal hematopoiesis. Probably, at greatest, only about 5% of those patients get any type of blood cancer. So, 95% of patients can have these genetic changes in their blood and not even know it; and it really is the other factors, we think, that are leading to their expansion and the disease development that we really need to learn so much about.

Dr. Greenberger: I should add at The Leukemia & Lymphoma Society, this is why we have heavily invested in not only CMML, but also what sets the stage for CMML or these leukemias because these mutations that could be just sitting there for years or decades are typically the same ones that are found in the disease-, usually in a constellation of multiple changes. But how do these changes occur? What do they actually do? Are certain changes worse than others? Or do certain changes progress faster, accumulate more over time than others? These are some of the things that we are investigating; and beyond that, the thinking about, well let's say that you have

this. You're a normal healthy person with these mutations. If and when do you treat? Would that be harmful? Would that be beneficial? Might we intercept from conversion over to a leukemia? These are some of the things that we've been studying.

Elissa: Wow, yeah, that's really interesting to hear that genetic mutations could be there for decades before they might even cause an issue or they might not cause an issue.

So, now that we've talked about the basics, let's talk about treatments. What are the current treatments for CMML?

Dr. Padron: Yes, so we can start off by discussing what the FDA-approved treatments are, but it's a little tricky with CMML because the FDA approves treatments, namely this class of medications called hypomethylating agents. They include Vidaza®, Dacogen®, Inqovi®. Their approval was based on studies that the vast majority of patients enrolled in this study actually had MDS. Because they were approved a while ago, it carried the CMML diagnosis with it.

And so while they're FDA approved, and we know that they can help with certain aspects of CMML, like blood counts, for example, recent studies from France have shown that, in terms of making people live longer or changing the trajectory of these progression events, that at least Dacogen, one of those hypomethylating agents, did not do that in this large, Phase III study. And so, yes, we have FDA-approved agents; but even those FDA-approved agents have their limitations, in part because it wasn't really studied in CMML.

And then after that, while there's a lot of promising clinical trials that we're involved in, it's really what we call a repurposing when we think about treatments for CMML. And what I mean by that is, sometimes there'll be a mutation in a gene – this is an example, IDH1 or IDH2 – that have a targeted treatment. And they are FDA approved for a different type of leukemia. We can often repurpose and use that. Now the challenges there are always whether the insurance will approve it. But certainly, if

they do, there are treatments that we can use and borrow for related diseases to help some of the symptoms of CMML.

Elissa: Okay. You mentioned Inqovi, and that is an oral medication, correct?

Dr. Padron: It is.

Elissa: One thing that patients may have some difficulty with when they take oral medications is adhering to taking it daily at home, right? I can speak personally to say that I am not the best with taking daily medication. How are you working with patients to make sure that they are taking these medications as prescribed, particularly when they have to take it at home versus in an infusion center or in the clinic, just so that they can effectively treat their disease?

Dr. Padron: Yeah. There's a few things there. So, one, when we're talking about this in terms of the clinical trial, it's very carefully monitored. At the end of every month, the remaining pills are counted, all that kind of stuff. So, all that is very well dissected as part of a clinical trial.

I would say a couple of things regarding not being completely exact with taking the medicines on time. Number one, unlike things like blood pressure which, obviously, can have long-term consequences, even diabetes. When you have a diagnosis of CMML, this is a serious, potentially life-threatening cancer. So, the stakes are really, really high.

And so, in my experience unless there's issues with dementia or things like that or caregiver support, generally the stakes are high enough to where patients remember to take their medications. And oftentimes, like, for example, Inqovi, it's not every day. It's five days out of a month that you take it.

Elissa: Okay.

Dr. Padron: Having said all that, the sort of prototypical example is this disease CML, so one M instead of two. In that one, there are medications that patients take for years and years and years, and it can keep their leukemia in control for a long time. It's what we strive to get to with CMML. And for sure, it's a problem there because they take it for a long time. It's one of the most common reasons for the medications to stop working is that people don't take it every day. But that isn't a problem in CMML, in my view.

Elissa: Okay. So, you've talked about the different treatments and that we really need more treatments for CMML. Now what is the current goal of treatment? Is it potentially curative, or are we really just looking at quality-of-life and hopefully reduce the progression of the disease?

Dr. Padron: Yeah, all of the above. Our goalpost changes, depending on how effective the drug is, right? So, for sure, curing the disease is our number one goal and priority.

But we recognize that, and I think this is being more and more recognized across cancer drug development, is that oftentimes curing a disease comes at a cost. There's toxicity. There's a lot of side effects that can have long-term consequences. Think of a bone marrow transplant. It is a curative, amazing treatment; but patients can have lifelong graft-versus-host disease (GVHD) and things like that. So, while curing the disease is the ultimate goal, it shouldn't be the only goal.

So, the most important one to me is, is your quality of life maintained? Are you able to do all the things that, you know, you need for daily living, to be happy? If you can do that, I think that's a huge win. And we often do for a period of time.

The other area that I think is really important, and we talked about this a little bit, is this isn't like diseases where only a small fraction of patients will end up dying from it. Unfortunately, in CMML, most people who have it, that's the thing that's going to cause them trouble, whether that be in the near future or in a long time.

So, if we could intercept the disease early on and keep it at a state in which people are happy, healthy, and can do what they need to do, I think that would be as important as "curing" them of the disease.

Elissa: You mentioned transplant earlier. Is stem cell transplant an option for CMML patients?

Dr. Padron: It absolutely is an option for CMML patients. But, the biggest challenge is that only a fraction of patients get to a transplant. In part, that has to do because of the eligibility requirements. You have to be strong and healthy. There isn't really an age cutoff, but there is a fitness cutoff.

So, if you have other issues like bad kidneys, bad lungs, you just can't have that procedure. But, we know that there are a subset of patients that can be cured with a transplant; and so, in the right patient, with high-risk disease, it absolutely should be considered.

Elissa: Okay. Now that we've discussed current medications, let's talk about the new CMML Initiative that is supported by LLS. Could you tell us about it and why it's needed?

Dr. Padron: The short answer is, it's needed because we have very few tools in our toolbox to treat CMML. And so, while there's so much we need to learn about, as you said, how the disease progresses. We need to learn about how it starts. We need to learn the underlying biology more effectively. But above and beyond all of that, the most important thing is we need effective treatments with minimal toxicity that can either keep patients stable and doing well for a long time or cure the disease. And that's, to me, the number one reason why it's needed.

Dr. Greenberger: Yeah. So, let me give you a little bit of perspective, why The Leukemia & Lymphoma Society got involved. First of all, we recognize, as Dr. Padron just mentioned, high unmet medical need with no really good therapies that are

available today. Maybe some that can keep the patients in check for a while, but really not ideally effective. Not even close.

This is a rare leukemia. About, let's say 1,300 new patients a year, which in itself creates a lot of issues. But one thing that it clearly creates is the lack, of motivation from the manufacturers. So, high unmet medical need with a low interest from the commercial side; and that sort of prompted us to say this is something that LLS can really contribute to as a nonprofit. And also, where the government may say, "Sort of interesting, but we've got so many other priorities. This isn't really something that we can put a lot of money behind."

On the other hand, it just so happens that LLS was approached by the Mike & Sofia Segal Foundation, and the foundation is laser focused on developing better therapies for CMML; and we're very fortunate that the foundation has provided $17 million to LLS to advocate for the whole scope of support of patients, understand the disease, better therapies, getting access to the disease, developing what is the criteria for a good drug? How do we know that a good drug is going to be effective and useful in the long term? So, the whole spectrum can be assisted with that money provided by the Segal Foundation.

And so, that's where LLS really got involved. We're very fortunate to work with people like Dr. Padron and, honestly, there's not that many specialists across the country and across the globe who are really focused on CMML. And so, the goal is to bring these people together with the financial support behind it and to bring in the pharma companies to develop these drugs to ultimately get better therapies.

Elissa: Wow. Could you tell us why the Segal Foundation decided to really be laser-focused on CMML?

Dr. Greenberger: Obviously, the foundation has a medical interest in CMML. CMML is in his family. The good news for us is he's got the vision to support better therapies. And he's invested in LLS, not only for CMML, but in rare diseases as well because he

recognizes that supporting development of rare diseases, whether it be blood cancer or otherwise, is something that philanthropists can do and do it outstandingly well.

Dr. Padron: I'd echo that statement about rare cancers. If you look at the National Cancer Institute (NCI) definition of rare cancer and you combine all patients with cancer who meet that definition of a rare cancer, that's 30% or more of all patients who get cancer. So, while in any one instance, like CMML, the numbers may seem small. Really coming up with mechanisms to get therapies for these rare cancers is going to impact a huge number of patients that have cancers.

So, it is really important for that message to be loud and clear, that rare cancers need support because a lot of us have it.

Elissa: Yeah. We interviewed Dr. Pemmaraju on CMML a year ago. And one thing he said in the podcast was that it may be a rare cancer, but it's not rare to the patients. It's not rare to the caregivers. They need help. They need treatments, and so it is important.

Dr. Greenberger: Yeah. Our understanding of CMML is emerging; but it's very clear that some of these changes that happen in CMML patients and mutations are happening in other cancers as well. And, even the drugs to treat it, the way these drugs work in terms of controlling the ability of DNA to ultimately make proteins and the mechanisms that control it, we've been studying those things for decades.

And, honestly, the ability of drugs to control that readout of the DNA is something that is important in many, many different blood cancers. And so, even our understanding of CMML and the underpinnings of it is going to tell us something much wider about leukemia, and probably the drugs are going to help us actually figure out how to control the readout of DNA to ultimately cause malignancies.

Elissa: Wow, that's really exciting. Let's go into clinical trials. So, are there challenges with getting new therapies for CMML from clinical trials to regulatory issues?

Dr. Padron: Oh, absolutely. Several levels of challenges. Some of them are real and are clear challenges that are inherent with this disease. But frankly, some of them are not, in my view. And so, for example, I almost weekly have conversations with pharmaceutical companies about potential drugs for CMML. And ultimately, while there's a lot of excitement and while there isn't even the agreement to fund initial studies for CMML, the bar of those drugs has to be so high because there's a notion that, as Dr. Greenberger said, whether it be the economics or the logistics don't work out when you have a "rare disease" like CMML.

I think Dr. Greenberger and LLS have done a fantastic job of making the case. But we always say that there are so many examples of drugs, in even rare diseases, that have been wildly successful. The medications that I mentioned in CML, also by National Cancer Institute a rare cancer, actually increased the number of people alive with it. That meant more people were taking it for more time. So, if you come up with a drug that actually works well, there's going to be more people taking it because they're going to be alive longer. So, there's that discussion that we always have with pharmaceutical companies and with varying degrees of success.

But then there are also real impacts too. This isn't prostate cancer or breast cancer where you can find thousands of patients. It is a rare cancer, although again, I always like to stress, it's not so rare. It's not different than a lot of blood cancers that have already had drugs approved. But it is rare, and so, yes, accruing clinical trials is a challenge. You need multiple sites, and so that is a clear challenge.

And another challenge, which has been partially addressed, is coming up with a consensus of what is working. What does it mean that a drug is working? What are

the criteria for that? And, a group of us, led by Michael Savona have published, what we think the response criteria would be.

But, because there is as yet not one single drug that has been FDA-approved for CMML only, we don't know if those response criteria will actually be the benchmark or the goalpost that the FDA or other regulators use. And so, the last thing I'll say is, again, challenges on the regulatory side are that, you know, I've had many discussions with the FDA. They're certainly engaged. They recognize the unmet need. But the challenge is when pharmaceutical companies, investigators are looking at the landscape, there is no trial that they can model and say, "Okay, if we do it like this, it has already been approved and, therefore, we've got a shot." It really just is open ground for that first drug to be approved. And I think after that, there'll be a lot more information for clinical developers in the regulatory space.

So, there are lots of challenges, but the good news is that on all of those fronts, I think we're making headway. And I think, part because of the huge commitment that The Leukemia & Lymphoma Society has placed, because of the Segal Foundation. I've been working on this disease for well over a decade. And today isa time in CMML research where I receive the most interest from pharmaceutical companies, where there's more of my colleagues interested in the disease, and so I really do see a bright future for CMML drug development. So that's the good news.

Dr. Greenberger: And part of our responsibility at LLS is to bring the clinical community together because it's a rare disease, because trials have to be run in multiple sites, because the definition of a successful drug is going to have to be defined by the clinicians and agreed to by the FDA. And even what an approval trial might look like. Could it be a single drug or combination, let's say, with azacitidine, and it doesn't require a comparator, or it does require a comparator? Now you've just doubled the size of the trial.

And by the way, what's the definition of a good response? Is it, "I can't find any blasts at a certain point, or is it Duration of response"? What is that duration of response that's going to be good? All these things need to be defined; and we need to educate both on the pharmaceutical, on the academic, and on the regulatory side what that is. And we're going to have to come to some consensus as these drugs go into development. And some of them are showing interesting data to say, what more do we need to prove that this is useful and safe, of course, in CMML patients?

Elissa: Yeah. Now, with so few people getting diagnosed every year, are there also factors inhibiting participation in clinical trials?

Dr. Padron: Yeah, absolutely. So, the most important part of the logistics of any clinical trial is what we call the accrual rate. How fast can patients be enrolled on the study? There's a direct link between accrual rate and incidence or how often people are diagnosed with the disease. Of course, the more likely it is that someone has a certain type of cancer, the higher the accrual rate could be for those cancers. And then, as I said earlier, it requires more logistic investment because where maybe there's a more common cancer in which with just three cancer centers, you can enroll lots of patients to help answer a question, for CMML and other rare cancers, you have to have a lot of participating cancer centers together to come up with the numbers needed to answer the question. And then there's costs. Every time you open a different site, there are start-up fees, there are site fees. And so, the costs of the clinical trial per capita goes up for rare cancers, as well.

Elissa: Right. So, what do you both see for the future of CMML treatments? Where do we hope this CMML initiative will go?

Dr. Padron: Yeah, I'll tell you what my A+ result would be for this initiative. Number one, that we have the first FDA-approved treatment for CMML. Whether it's a home run or not, I would love for it to be something that cures CMML. But I really do think once that first drug is approved, the floodgates will open, people will realize that it's

important, that it's economically viable, and many more will follow. So, if we can get that first one approved, I think a lot of good things will happen.

And then as I said earlier, I think one of the most critical things, and something we're really interested in, is when to start the treatment. Because right now, because nothing changes, survival, progression, we start treatment when people start feeling bad. But because we know most people will feel bad, even if they feel good now, maybe weeks, months, and some people thankfully years, but at some point in general, people start having symptoms. Why couldn't we have treatments that prevent that from happening, that mitigate that? And that's something that I'm really interested in; and I hope that timing question is something that we can address during this initiative as well.

Dr. Greenberger: I think also a better molecular understanding. We know what some of the targets are. We know what some of the bad actors are. We don't have drugs for these yet in some cases, and they're being developed in some cases even where these same mutations occur in other diseases and try and develop therapies there and bring them into CMML.

But beyond that, we have a lot of technology behind us that we can say, "Hey, what's unique on the surface of these CMML cells, because we know that we can develop basically immune-directed therapies for other diseases to hone in on these tumors and kill the tumor cells?" So, we could use the new technology that we have if we can identify unique markers on these CMML cells to wipe them out, as we've done, for example, in diffuse large B-cell lymphoma where we basically activate the immune system to kill diffuse large B-cell lymphoma.

So, I think there's a lot of opportunity here. It's harnessing the technology; it's bringing the pharmaceutical companies' interest; and I think as Eric is right, put one over the top. Get it through the goalpost and say we can do this; and now we have a benchmark that's going to be very valuable for the whole CMML community.

Elissa: Yeah, I think that is a great first goal to have. Get one past and approved.

Our final question today for both of you, on our patient podcast home page, we have a quote that says, "After diagnosis comes hope." What would you say to patients and their loved ones to give them hope after a diagnosis of CMML?

Dr. Padron: Yeah, what a great question. I think, firstly, despite what I said about patients ultimately having symptoms and that most patients, unfortunately, will succumb to this disease, there's always hope. There's so many examples in my clinic.

I'll give you one of a patient of mine who was diagnosed with CMML, was told, appropriately so, that he had a life-threatening disease. But it was five years before he needed treatment, and in those five years, did things that he would have probably not done had he known he didn't have CMML. He traveled the world and did a lot of things that perhaps he wouldn't have thought of before.

And so, I think having a diagnosis of CMML shouldn't prevent you from having a great quality of life. This isn't something that causes a ton of pain. This is something that is extremely serious, but in many patients can stay dormant for a while.

And then I couldn't agree more with the link of having a diagnosis and having more hope. Once you know what you have, once you open the door and you see the monster eye to eye, it's not as scary anymore. And when you connect with someone who knows what CMML is, who can tell you with some confidence that this is what we're going to do for you to make you feel as good as you can, I do see that there comes quite a bit of hope from that. It's something that I strive to help do, and I think what The Leukemia & Lymphoma Society is doing gives me personal hope because working on this disease for 10+ years, having an organization like LLS putting wind to our sails, is only going to do great things; and we're already seeing that.

So, I would just tell CMML patients just hold on. In my opinion, there will be an FDA-approved drug for CMML soon. And so, there's tons of hope.

Elissa: Wonderful.

Dr. Greenberger: Yeah, from my perspective, what we've learned, and certainly after being in the cancer field for 38 years, is the development of new drugs is around the corner; and what we've done, for example, in chronic lymphocytic leukemia (CLL) is multiple drugs have been developed. Nature is incredibly complex and smart, and you'll get a drug that'll be effective and then it won't be effective later on. Come up with a second drug, and the third drug, and the fourth drug, to understand how the system works, how to get around it.

Our strategy at LLS is to place multiple bets, because we recognize we don't know which drug might work out best compared to the other. But by placing multiple bets, that's a strategy that has been a winner for us over and over again. That's what we're doing in CMML, and I expect that we will have a new drug; and then we'll have drugs behind it.

And not only that, the level of interest will go up in CMML. You'll probably even see the incidence of CMML go up because people will recognize that this is a disease by itself and has been misdiagnosed or underdiagnosed, and so you'll probably see that as well.

So, I agree with Eric. Hang in there. We're working as fast as we can, and things look promising on the horizon.

Elissa: I love it. A wonderful message of hope for patients and their loved ones who are affected by CMML.

Well, thank you both so much, Dr. Padron, Dr. Greenberger for joining us today and sharing all about this really exciting initiative; and I am really looking forward to seeing where this will take us. And getting that first goal of a treatment approved and then going from there and keep on going.

So, again, thank you both so very much for joining us.

Dr. Padron: Thank you, Elissa. We appreciate it.

Dr. Greenberger: My pleasure.

Elissa: And thank you to everyone listening today. *The Bloodline with LLS* is one part of the mission of The Leukemia & Lymphoma Society to improve the quality of lives of patients and their families.

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In addition to the Lounge, we could use your feedback to help us continue to provide engaging content for all people affected by cancer. We would like to ask you to complete a brief survey that can be found in the show notes or at TheBloodline.org. This is your opportunity to provide feedback and suggested topics that will help so many people.

We would also like to know about you and how we can serve you better. The survey is completely anonymous, and no identifying information will be taken. However, if you would like to contact LLS staff, please email TheBloodline@LLS.org.

We hope this podcast helped you today. Stay tuned for more information on the resources that LLS has for you or your loved ones who have been affected by cancer.

Have you or a loved one been affected by a blood cancer? LLS has many resources available to you – financial support, peer-to-peer connection, nutritional support, and more. We encourage patients and caregivers to contact our Information Specialists at 1-800-955-4572 or go to LLS.org/PatientSupport. You can find more information on

CMML at LLS.org/Leukemia. These links and more will be found in the show notes or at TheBloodline.org.

Thank you again for listening. Be sure to subscribe to *The Bloodline* so you don't miss an episode. We look forward to having you join us next time.