LEUKEMIA & LYMPHOMA SOCIETY®

THE BLOODLINE WITH LLS

A PODCAST FOR PATIENTS AND CAREGIVERS

Episode: 'Patient-Doctor Perspectives: Hope in the Uncertainty of AML'

Description:

Join us as we speak with Charles Huang and Dr. Gabriel Mannis in honor of AML Awareness Day (April 21st). In this episode, Charles tells us about his treatment for AML, participation in clinical trials, and shares about his struggle to find a bone marrow donor as an Asian Pacific Islander. Charles then turned his struggle into legislation to make it easier to join a bone marrow donor registry to save lives. Dr. Mannis, of Stanford Medicine, shares about the latest advances in AML research, from clinical trials in Chimeric Antigen Receptor (CAR) therapy to medications that reduce graft-vs-host disease (GVHD). With research advancing quickly in the field of AML treatment, patients and caregivers are given reasons to have hope after the uncertainty of a diagnosis.

Transcript:

Elissa: Welcome to *The Bloodline* with LLS. I'm Elissa.

Lizette: And I'm Lizette. Thank you so much for joining us on this episode.

Elissa: Today we will be speaking with Charles Huang and Dr. Gabriel Mannis. Charles is a career prosecutor in Silicon Valley, California, and an acute myeloid leukemia, or AML, patient. He was diagnosed with AML in November of 2019. He underwent chemotherapy and participated in numerous clinical trials at Stanford Medicine and then, unfortunately, relapsed in April of 2021. After an extensive search for a donor match, he received a bone marrow transplant in July of 2021 and is currently in remission. A husband and father of three daughters, Charles is now using his AML experience to advocate for others, focusing on passing Charlie's Law which allows Californians to easily enroll in bone marrow registries when applying for a driver's license or identification card at the DMV (Department of Motor Vehicles).

Dr. Gabriel Mannis is an Assistant Professor of Medicine in the Division of Hematology at Stanford University School of Medicine and Medical Director of Stanford's Inpatient Leukemia Service. He specializes in the treatment of acute myeloid leukemia, high risk myelodysplastic syndromes or MDS, and other hematologic malignancies. As a clinical scientist, Dr. Mannis divides his time between caring for patients, teaching trainees, and researching novel therapies in multiple clinical trials for AML and MDS.

Currently, he serves on the National Comprehensive Cancer Network AML panel, helping to write evidence-based guidelines for how AML is best treated. In this episode of our *Patient-Doctor Perspectives* Series, we will be discussing the latest advances and treatments for acute myeloid leukemia and the experiences of one patient through multiple treatments, the search for a bone marrow donor, and his advocacy for future blood cancer patients.

Welcome Charles and Dr. Mannis.

Charles Huang: Hello, Elissa and Lizette.

Gabriel Mannis, MD: Hi, guys. Thanks for having me.

Elissa: So, let's start by learning a little about each of you. Now, Charles, it seems you're very active in your community as a prosecutor and also you cofounded the National Asian Pacific Islander Prosecutor's Association [NAPIPA]. Tell us a little about that and other parts of your life.

Charles: Sure. I grew up in the Bay area. This is home for me; and so growing up I wanted to help people. And since I like to talk a lot, naturally, I went to law school; and I wanted to help the community by becoming a prosecutor, by keeping the streets safe, and really do justice for those who have been either charged negligently so we can free them or keep the really dangerous bad guys in a secure facility, so they don't hurt people in our community. And so I've been able to do that, and through those experiences, I learned that there's not a lot of diversity in the prosecutorial profession.

And Asian Pacific Islanders like myself are few and far between in the prosecutorial ranks.

So, I wanted to increase the diversity in our profession to reflect our community because I feel like having the diversity to reflect our community is really another way to bring about true justice in our criminal justice system.

I founded this organization that has about 700 members in seven chapters. It consists of prosecutors, judges, law students, and those who support kind of a greater diversity within the criminal justice system. And every year we have a scholarship banquet encouraging diverse candidates who are seeking jobs to become prosecutors in the future with the goals of diversity and justice in mind. So that's kind of what we do, and I found it to be very worthwhile.

Lizette: Wow, that's really great to hear. It is important to kind of mirror your community, right, when you're providing services to the community.

Charles: That's the idea, exactly.

Lizette: Great. Well, Dr. Mannis, let's go to you. What got you started in the field of medicine and then studying AML and MDS?

Dr. Mannis: Yeah, well first I just want to say thanks to the LLS for inviting us on and for running this program, which I think is really valuable for patients out there. And I want to especially thank Charles for being here and sharing his story which I know is not the easiest thing in the world. So, thank you guys.

I knew I wanted to be a doctor from a very young age. My father is an ophthalmologist. My mother is in education and really were great role models in terms of inspiring me to help take care of others and to advance the science.

I got interested in science very early. I actually met my wife when we competed against each other in a national science competition when we were in high school. So

my interest in medicine started very early. That being said, I really didn't have leukemia on my radar until relatively late when I went through medical school and through my internal medicine training. I really loved everything. I liked primary care. I liked infectious disease. I liked palliative care, which is often taking care of people at the end of their lives.

And so I really didn't have a real sense of what I wanted to do until I did my first rotation on the leukemia transplant unit where I really discovered that as a leukemia doctor, you essentially become the primary doctor for patients with really complicated medical problems who are often dealing with the most stressful situation of their lives. And you get to see them in the hospital. You get to see them in the clinic. You get to follow them over months and years, and at the end of the day, there are patients that you get to cure of their cancer. And so for me it has been a really rewarding journey.

Lizette: And that's great to hear. I like the story of how you met your wife. Our main focus today is on acute myeloid leukemia or AML. So Dr. Mannis, can you explain to our listeners what AML is?

Dr. Mannis: Sure, so leukemia, in general, is a term describing a blood cancer; and all of our blood is made in our bone marrow, and so it's essentially a cancer of the blood and the bone marrow.

I often get asked by patients what stage is their leukemia; I think an important thing to know is that because leukemia is a cancer of the blood and blood goes all throughout the body, you have bone marrow throughout all of your bones, there really aren't stages for leukemia.

As far as AML, acute myeloid leukemia, there are, of course, many different kinds of leukemia. And the A, the acute part means that this is a kind of leukemia that typically comes on quickly. Most patients are feeling generally normal, generally well; and then within a matter of weeks or maybe just a few months, things go from normal to very abnormal. So it's a fast-moving, aggressive type of leukemia.

The M, the myeloid part, there are really two branches of the blood system. There's the lymphoid side and the myeloid side. And so you may know of other types of leukemia, CLL, which is a lymphoid type of leukemia, a chronic form; CML, which is chronic myeloid leukemia; AML is an acute leukemia that affects the myeloid side. And what does that mean, the myeloid side? This is a cancer that affects the red blood cells, the platelets, and the white blood cells. Those are the three main components of our blood system. And in myeloid leukemias, there is a cancerous blood cell that ends up growing out of control and typically crowding out the normal red blood cells, platelets, and healthy white blood cells.

And so the downstream consequences of AML or acute myeloid leukemia are that patients typically are very immunocompromised. Their white blood cells don't work to help prevent them from infections. Their red blood cells are typically low, which we commonly know as anemia. And the platelets are low which often results in bruising and bleeding; and so that in a nutshell is AML.

Elissa: I'm curious, you talked about no staging for leukemia, particularly for AML. All of the AML patients, I'm sure, listening right now have heard the word "blasts" and that they have a certain percentage of blasts in their bone marrow. I'm an AML patient myself. I was diagnosed at 20% blasts. If there's no staging, does it matter what your percentage is as far as how many blasts that you have in the bone marrow as far as your prognosis or quote/unquote "catching it early"? Does that matter at all?

Dr. Mannis: The exact number doesn't necessarily matter. I should say that typically we define leukemia by a blast percentage of 20% or more. So it sounds like you were right at the cutoff there.

But, from a practical standpoint, whether you have 20% blasts, 50% blasts, 80% blasts, it's sort of a binary thing. Either you have leukemia, or you don't. In terms of catching it early, it is certainly possible to catch it early. And when I say catching it early, I mean before having any of the serious consequences of the AML itself like

serious infection or serious bleeding. But the specific blast percentage is not necessarily the most important factor in terms of how people are going to do.

Elissa: Thank you. Now, Charles, you were diagnosed with AML in November of 2019. What were the signs and symptoms that led to your diagnosis?

Charles: It's funny you mention that based on Dr. Mannis's description. So I remember I was in the middle of a murder trial in August, and I caught a cold from my daughter. And that cold never went away. It just continued, runny nose, congestion, and it lingered on and on through the course of that trial. And I finished it, at the end of November; and something was just not right in the sense that I just couldn't feel well, and then headaches started to develop every day. And I would take Tylenol® or some sort of pain relief quell the headaches.

The headaches started to get compounded with fatigue. I like to play golf. And I remember just not being able to walk the golf course initially, to the point where right before I was admitted to the hospital, I couldn't walk down a flight of stairs.

And my head was so heavy that my neck didn't have the strength to kind of keep my head up; and so when I went to the doctors before the AML diagnosis, I was told, I just had really bad posture and I needed some physical therapy. And I had a really stressful job, and I needed to take some time off; and I just knew that wasn't right.

So eventually they said, "We don't know what's happening. Would you like a blood test?" And I said, "Yes, please give me any kind of test to kind of tell me what's happening." And when they did, I remember them telling me, " Would you mind coming back tomorrow to do another blood test because I think our machine is broken because these numbers don't look right? Your white blood cell counts are not right, and so come back tomorrow so we can run the test again." And they ran the test again, and they're like, "No, it's not our machine. It's you."

Elissa: Never want to hear that.

Charles: Yeah, I just knew that was really bad. And I remember hearing that initial diagnosis; I was so frightened. And to Dr. Mannis's point, I wanted to thank LLS and Dr. Mannis for the care and treatment I received. I remember having that diagnosis, and I had to wait 2-1/2 weeks to see somebody because they had told me, "Don't worry, it was chronic, so you have time." And so during that time, I was like, oh, my God, leukemia, what is that? That is so frightening. And I would look at the LLS resources, the podcasts and everything. You guys really helped me in a tremendous state of disarray and, and franticness and it really brought, provided me that information and the resources to help me kind of get to the next phase to get to Dr. Mannis for my treatment. And so I'm ever so grateful for everyone on this podcast, for being here today to be able to tell my story.

Elissa: We're so glad to hear that.

Lizette: Yes, definitely. Now I guess they did find that it was acute. Did you start treatment right away? I know that in the introduction we did mention that you did participate in clinical trials. So what was your treatment course?

Charles: So I went to see the CML doctor. I remember it was like a 5:00pm appointment; and I walked in and he said, "I can't help you. Everything that you have here shows that you have acute, you have AML. I'm a CML doctor. I can't help you." And I remember he was texting another doctor to try to get me a bone marrow biopsy; and he said, "Your numbers look really bad. You need to go to the hospital immediately." Like right now, check yourself into Stanford at the Emergency Room; and you need to go.

And I said, "Come on, doc. I've been dealing with these issues since August. I'm going to be okay. Give me some time. I need to say goodbye to my wife, take care of my kids, and some of these things." And he said, "No, you need to go now." I begged and pleaded with him, and he let me go in on Monday. Stay on a Friday afternoon and go in on a Monday.

And I remember that weekend, I couldn't get out of bed. I just kept thinking to myself, I should have gone to the hospital. I should have gone to the hospital when he told me to because I couldn't get out of bed. And I was just so weak. I don't even know how to describe that feeling. But it wasn't just fatigue. It literally was this is what it feels like to be dying, I think. And as far as the course of treatment goes and the type of clinical trials, I think Dr. Mannis would be in a much better position to discuss that than me.

I met Dr. Mannis, and I had full faith and trust in his advice and suggestions. And he said, "If this is a good plan, I'm going to go with it." So I'll just defer to Dr. Mannis on that.

Dr. Mannis: Yes, so Charles, for his initial treatment, was not on a clinical trial. This was sort of a standard treatment; and when we think about treatments for AML, we sort of lump them into two different categories. And one is sort of the more intensive treatment that we reserve for younger people. And when I say younger people, typically under the age of 60 versus less intensive treatments which we use for patients over the age of 60 or those who have other health problems.

Charles is a healthy guy. When I first met him, it was clear that he could handle an intensive treatment. And so he got a 7 +3 based treatment and 7 +3, probably many of us are familiar with it. It's a combination of two different kind of old school chemotherapy medicines that have been around since the 1970s. The idea is that it's sort of like a control/alt/delete for the bone marrow. It shuts everything down. You wait three to four weeks and hope that when it reboots that it reboots with the good stuff.

We also gave Charles a newer treatment, a drug called gemtuzumab ozogamicin, which is a mouthful; but it's a newer treatment that is an antibody, which has a little smart bomb linked to it, and so it hooks onto the AML cells. When it hooks on, it gets internalized into the cell; and it releases the smart bomb into the cell. And so Charles

got a combination of these three medicines for his induction. He was in the hospital I would say about a month. And fortunately, it worked for him; and he went into remission. Although as he can probably attest, it was not the easiest month.

Charles: That was not fun. So after the induction treatment, I also received a clinical trial to get into re-remission prior to transplant; and I think Dr. Mannis can talk about that. And the other clinical trial I received was during my bone marrow transplant. The purpose of that was to minimize the risk of graft-versus-host disease post bone marrow transplant.

Elissa: So was it just the standard chemo treatment up until the relapse? Did you do the standard chemo treatment plus the additional drug that you just discussed up until the point that he relapsed and then needed the bone marrow transplant?

Charles: Yes.

Dr. Mannis: In general, when we think about treating AML, we categorize it really into three categories. There's a good risk group, which is sort of a misnomer because all AML is bad. But there's a better group of AML. There's an intermediate risk group and a poor risk group. And when Charles was diagnosed, he was in the good risk group. And the implications of being in that good risk group are that we think that we can cure half or more of patients with chemotherapy alone. And so Charles got induction chemotherapy and then several rounds of what we call consolidation chemotherapy. At the end of that, there was no detectable leukemia. His blood counts were normal. He felt well, and so we transitioned into this period of just sort of watch and wait where we were checking labs every month, making sure everything looked good. And unfortunately, a year later, we found that the leukemia had come back.

Elissa: Now you talked about the different risk groups. Those are generally categorized, often based on a genetic mutation, correct? I had inversion 16. I'm not

sure what Charles ended up having, but they find the genetic mutation and then you're kind of put into a category as far as what could potentially work for you?

Dr. Mannis: Exactly. There are two main factors that go into determining both the prognosis for an AML patient but also for the treatment. And one set of factors are the patient factors in terms of their age and their other health conditions, but the other main category are the genetics of the AML itself. And so we know that AML is really not one disease but actually dozens if not hundreds of different diseases, based on their genetic makeup.

And so we look at the chromosomes in the AML cells and the genes in the AML cells. And there are a few chromosomal changes, including inversion 16. There are a few gene changes, including the NPM1 gene, which is the gene that Charles had that was mutated. And those put people into the better risk group.

For those patients who were not in the better risk group or potentially who were over the age of 60 and can't receive intensive type treatment, for those patients we think really the only chance of curing their leukemia is with a bone marrow transplant.

Lizette: So is that why certain folks get bone marrow transplants and others don't, because not everybody with AML, as Elissa said, will get a transplant.

Dr. Mannis: Yeah, so there are a lot of reasons why people may not get transplants. To get a transplant, first you have to be in remission. So the leukemia has to be under good control to get the benefit of a transplant. A person has to be healthy enough for a transplant, meaning they have good heart function, kidney function, liver function. Age is not a strict criterion for a transplant, but typically, transplants are limited to patients, under the age of 70, 75, although that number is inching upwards and upwards as we get better and better with our transplant technology.

Elissa: Now, Charles, let's move forward to your relapse and then bone marrow transplant. When a patient needs a transplant, there is a search done in national and

international registries. But you didn't initially find a donor, correct, and that must have been really scary. Could you tell us about your search for a donor?

Charles: Sure. It was really scary. I relapsed in April. Was pretty devastating. I called Dr. Mannis in a panic, and he calmed me down and we went to the hospital, and like Dr. Mannis mentioned, the first thing is to get into remission again. So we went through another round of chemo also with a clinical trial, and I was lucky enough to get into remission. And then the search for a donor started. And that's when I really learned that minorities, Asian Pacific Islanders, Blacks, Latino, we have a much smaller chance of finding a bone marrow donor match because so much of it is genetically related than Caucasian, than White.

And as the search grew, there were no matches for me in the entire global database. And it was just moments of despair. I remember sitting in the hospital during COVID by myself because family wasn't allowed in. My wife came in, but no kids. I wasn't able to see them and thinking to myself, okay, so even after I get into remission with chemo, really the next step is really vague and really uncertain. And because I had a very unique, I guess, genetic subtype or something, there was one match in the entire world, and it was my brother. But-

Elissa: Oh!

Charles: -my brother was also a cancer survivor, so there was extreme hesitancy to use him as a donor.

Elissa: Yeah.

Charles: So at that moment, I was in the hospital by myself. Lots of despair. And I just said, "Look, it shouldn't go down this way." I started drafting legislation to say, "if the California DMV allows people to volunteer to become organ donors, why not for bone marrow as well?" So the idea of Charlie's Law came in when I was in the hospital. As a lawyer, I'm drafting a bill, looking at the law saying, "Hey, if people can

donate their organs after a car crash, why not be able to donate and be a bone marrow donor at the DMV and just check a box?" If you're interested in becoming a volunteer, check the box in the DMV, then Be The Match will then send you a kit. You swab it in your mouth, and you send it in and you're in the database. Given the diversity of California, that's going to help everybody. It's going to help all the minorities and the non-minorities.

And so that's kind of the genesis of Charlie's Law and where it came about by increasing the available donor base for folks who can be bone marrow donors. We tried to pass that last year, and it made it through the Transportation Committee, but it did not make it through the Appropriations Committee because they're worried about how much money it's going to cost the state. I don't know how much you can put on the price of saving people's lives, so I'm not really happy with that, but Assembly Member Evan Low, from the Bay Area has resubmitted this bill and it's AB1800 this year to try and get it through again. So we're going to keep trying, and we're going to keep trying to save lives by increasing the donor pool through the California DMV.

Lizette: That does make sense. It really does. I know that when I got on to the registry, I was wondering why isn't everybody getting onto this registry for Be The Match? It's great. I love this idea. Love it.

Charles: I forgot to mention LLS is now a proud sponsor and endorser of this bill as well.

Elissa: Wonderful.

Charles: So when the time comes, hopefully our audience from LLS can call the Appropriations Committee chair and let him know how important this bill is and ask him to pass this bill from the Assembly. And we can get it over to the Senate side and continue to work there to pass this bill.

Elissa: That's great. we'll make sure to put an LLS advocacy link in the Show Notes for our listeners who want to get involved on the policy side and could really help out with that. And I think it's such a great idea, and we really do need more donors. Seems like everybody that I know gets a donor from Germany. I don't know if they have some robust registry over there, but I feel like everybody I know gets a donor from Germany.

Charles: It's compulsory in Germany.

Elissa: Well, there you go.

Charles: So everyone has to be a donor in Germany.

Lizette: Yeah. Well we have to bring that over to the United States with our strong advocacy team here at LLS. I know that Charles, you mentioned that it is harder to get a donor for people of color, for minorities. Dr. Mannis, is there a reason for this?

Dr. Mannis: Yeah. finding a match, we know about blood types. There's A, B, O. we all I think are sort of familiar with that. To find a bone marrow donor, there's essentially a bone marrow type that we call HLA, human leukocyte antigen, and it's much more complicated than the red blood typing system.

And part of the issue is that people of color are underrepresented in the registry, so it is a predominantly White registry at this point, although that is shifting. But that's not really the main issue. The main issue is that the people who are Caucasian of Western European ancestry, have a really sort of simple uncomplicated bone marrow type. And so it's much easier to find matches for Caucasian people of European decent, whereas the bone marrow matching the genetics of this HLA for people of color are actually much more complicated, much more diverse. And so even if we had equal representation within the registry, it would still be more difficult to find matches for people of color, which is why increasing representation is so important in these groups.

Elissa: Now, Charles, I just have to know, was your brother the donor or did you end up finding an unrelated donor?

Charles: Oh, yes. My brother did become the donor. I'm so grateful to my treatment team at Stanford. They ran my brother through so many tests to make sure that he was going to be safe and make sure that I was going to be safe, that at the end, after weighing the cost-benefit analysis, they decided to go ahead and use my brother as a donor. So my brother literally has saved my life and given me some extra time. And I'm so thankful.

Elissa: I'm so glad that he was a match and then that all worked out. And, again, for our listeners, we'll have information about Be The Match so you can sign up for the registry yourself. So, I hope everybody listening that is not a patient will sign up for the registry.

Now, Dr. Mannis, let's move on to talk about the latest advances and treatment for AML. So, since I was diagnosed in 2016 when there really were no new treatments for the past 40 years, I was still using that 7+3 that you talked about, since then there have been several new treatments to get approved and many more in trials. Could you tell us about the latest advances and maybe what is on the horizon that you're excited about?

Dr. Mannis: Yeah, it's been a crazy time for AML patients and for AML doctors. This 7+3 treatment that we talked about was first described in the 1970s. And from the 1970s up until 2017, there was really only one new drug approved in AML, so, it was this bleak landscape for both doctors and patients because we really had very few tools to treat patients. And so, with such a, tough disease as AML, it was really, really discouraging.

Part of my interest in AML was exactly because of that because there really was nothing there. And so my sense was that during my career, I had the opportunity to really try and advance the field. Little did I know that, from 2017 through now, there

have been nine new drug approvals for AML, which has really changed the landscape and really starting to move the needle for how patients are doing.

And one of the things that I think is important is that of those nine new drugs, five or six of them are targeted drugs; things that specifically target certain genes, certain proteins so that not only are these treatments improving the efficacy for patients, but they're also much less toxic. So, instead of this sort of nuclear approach where we just shut everything down, people lose their hair, they get sick, these are drugs that really can have very few side effects that people in their 80s, even 90s can take. And so that's been really exciting.

Charles mentioned that he has participated in several clinical trials with us, and I think that's an important message is that these advances have come because of patients who have been willing to get involved in these clinical trials. There are several new things on the horizon and they're all sort of informed by the increasing understanding of the science of the biology. I am a clinical researcher. My job is really running clinical trials understanding how these drugs work in people, but we owe a lot of credit to the basic scientists, as well, who are identifying the really basic cellular mechanisms so that we can find the Achilles heel and ultimately cure more people with AML.

Elissa: In one of our recent episodes, we talked about the trials going on and potential for CAR T-cell therapy, but also CAR therapy with natural killer cells. Could you talk a little bit about those?

Dr. Mannis: Yeah. So, CAR T-cell is certainly a hot topic. For those who aren't familiar with CAR T-cells, it stands for chimeric antigen receptor T-cell. So it's taking a patient's own T-cells, they're part of their immune system, and then engineering them so that they specifically seek out and destroy specific cells. And there have been CAR T-cells that have been approved for lymphoma, for myeloma, for ALL, which is a different kind of acute leukemia.

So far there has not been a really successful CAR T-cell for AML, and there're a variety of reasons for that. For a CAR T-cell to be successful, you have to have a target for that CAR T-cell and that target ideally would be only on the AML cells and not on any other cells. But if it's a target that is on AML cells and other cells, then those other cells have to be cells that you can live without because the CAR T-cells get in there, they expand within the body, it's a living drug – and it continues, hopefully, to seek out and kill off these cells.

And so the issue in AML is that we haven't yet identified a target that is only on AML cells. And, unfortunately, the targets that are on AML cells are shared by really important other cells, like platelets and red blood cells and neutrophils. And so while there are many AML CAR T-cells in trials, none are yet ready for prime time.

You mentioned NK cell therapies. Certainly, I think we are interested in AML in looking at other types of immune cells and immune therapies to try and cure AML. Bone marrow transplant fundamentally is the first successful immunotherapy. It's taking a donor's healthy immune system and using those immune cells to wipe out any leftover leukemia. And so there is precedent for immune-based therapies in AML. But unlike in myeloma and lymphoma and solid tumors like lung cancer and skin cancer, we really haven't seen immunotherapies be particularly effective in AML. But my hope is that, with ongoing research, we will find a successful immune therapy for AML and, ultimately, I think the goal is to put transplant out of business.

If we could find better treatments early on that could really wipe out every last AML cell, then maybe we could make transplant a thing of the past.

Elissa: And, hopefully, someday chemo too.

Charles: I second that.

Elissa: Yes.

Lizette: Yeah. But definitely it is exciting to know that there's so much more research and so many new treatments after having so many years, decades really, without newer therapies for AML, so it is an exciting time.

Now, Charles, on our patient podcast home page, we have a quote that says, "After diagnosis comes hope." Based on your cancer journey, what word would you use to complete that sentence, "After diagnosis comes"?

Charles: I think the most accurate word I would use in my experience would be uncertainty. And that has been the biggest obstacle that I've had to deal with through this journey just not knowing are things going to be okay? Are they not going to be okay? How much time do I have? What available resources and treatment options do I have? What if it fails? What if it doesn't fail? What if I'm able to not relapse? I just think that's just a very normal human reaction when you're dealing with this issue, and the fear of uncertainty has really made things difficult for me in this journey. And so that's the word I would use.

Elissa: Yeah.

Lizette: Very real. Very honest. Thank you so much for sharing. And like Dr. Mannis said, I know it's sometimes hard to share your story, your journey with others, so we really do appreciate that you were able to share your story with us today.

Charles: Of course, happy to help.

Elissa: Now regarding hope. I have a question to you, Dr. Mannis. So with the current treatments and those on the horizon, what would you say to patients and their families to give them hope after a diagnosis of AML?

Dr. Mannis: That's a great question. I think hope is an essential part this journey because, like Charles said, there is a lot of uncertainty, and so maintaining hope in the face of all of that uncertainty is really important. And I think like we discussed, not only have there been multiple new drug approvals in this disease, but they are drugs

that tend to have fewer side effects. We are now moving into an era where, we're thinking about combining these drugs, how to sequence them, and like in other cancers, like in myeloma, for example, where, even just a decade ago a newly diagnosed myeloma patient you might only say would have a couple years to live; now they're living, a decade or more. And I think we're right at that point in AML where the science is moving at a pace where things are changing month to month, year to year in terms of what is out there.

And so, not only do we have more effective drugs available, but as we get more and more drugs, we are increasingly focused on improving patients' quality of life, which I think in AML had not been a big focus, as recently as five, ten years ago because we just had these crude tools. And now that we have much more precision tools, I think the focus is shifting to not only how do we best cure patients but both for patients who are curable and for those patients who are not curable, how do we not just maximize the quantity of life but the quality of life? And so there are a lot of studies that are looking at those measures.

Dr. Mannis: I would just throw in a plug there that, things really are changing so rapidly so that, I would say the majority of patients who are followed at a sort of community center, have an oncologist in their community, I would say it's really important to seek out a consultation at an academic center where there's someone who is really up to date on the latest and greatest in AML because things really are moving so quickly. Even if it's just a one-time consultation just to get a sense of what tests should be done, are there new tests that can help detect even smaller amounts of leukemia, what we call MRD, (minimal or) measurable residual disease, are there new drugs out there, are there trials that they can participate in?

Oftentimes, the model now is that I have patients who are primarily treated by their local oncologist but that see me once in a while. Nowadays in the COVID era, we do a lot of video visits, so it's become much easier, I think, for patients to get plugged in to

an academic center where there's somebody who's really focused on AML and is sort of up to speed on all of the really fast-moving developments.

Elissa: Absolutely. It really is so important to get with a specialist, particularly with a disease like this, even if it is just a consult. So I think we're hearing more and more of that of local oncologists consulting with big academic centers and a specialist to make sure that the patient is getting the best treatment. So that is a very excellent point.

Charles: wanted to thank you for having me and just leave by saying that given the uncertainty, I think my advice to folks who are going through this journey is although there is uncertainty out there, you can always put yourself in the best position to succeed. And like Dr. Mannis says, seek out second opinion, go to a research center, do the things that you're supposed to do to increase your chances. And those are the things that we can control and, in this world of uncertainty.

Elissa: Well, thank you so much, Charles and Dr. Mannis, for being here with us today. It is so exciting to hear about the treatments on the horizon and really just how much has changed over the past few years in AML treatments, it takes a little bit for that survival rate to hike up. I know everybody listening today probably knows that AML overall has a fairly low rate of survival and so I'm excited to see over the next few years it really come out. It seems like there's so much better chance of survival and that's just really exciting. So I hope everybody listening today has that bit of hope in the uncertainty that there really is a chance of survival and things are changing so rapidly.

So thank you, again, so much for both of you for being here with us today. We really appreciate it.

Charles: Thank you for having me.

Dr. Mannis: Thank you.

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. To help us continue to provide the 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 your better. The survey is completely anonymous and no identifying information will be taken.

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 also find more information on acute myeloid leukemia at LLS.org/Leukemia. To learn more about signing up for the bone marrow donor registry, we encourage you to visit BeTheMatch.org. All of these links will be found in the Show Notes or at TheBloodline.org.

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