THE BLOODLINE WITH LLS

A PODCAST FOR PATIENTS AND CAREGIVERS

Episode: 'Patient-Doctor Perspectives: CLL and a Decade of Transformation'

Description:

Join us in this next installment of our series, *Patient-Doctor Perspectives*, where we explore a diagnosis from the view of a patient and doctor. In this episode, we speak to Dr. Larry Saltzman, a Chronic Lymphocytic Leukemia (CLL) survivor and physician researcher and Dr. Steven Coutre from Stanford Medicine. Dr. Larry shares his experience living with CLL, participating in LLS Team In Training events, and his current work with LLS studying patient outcomes and COVID-19 vaccine antibody response. Dr. Coutre then delves deeper into CLL treatments, responses to vaccines and what is on the horizon for new treatments and clinical trials.

*Please note that this episode was recorded prior to the rise of the COVID Delta variant and release of booster shots. We encourage patients to consult with your physician regarding COVID-19 safety and vaccines. Preliminary results have also been released for the antibody study and can be found in the show notes.

Transcript:

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

Edith: I'm Edith.

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

Elissa: Today, we will be speaking with Dr. Larry Saltzman and Dr. Steven Coutre. Dr. Larry is a chronic lymphocytic leukemia, or CLL survivor, Board Certified Family Physician, and Executive Research Director for LLS. Diagnosed with an aggressive form of CLL in 2010, Dr. Larry went through multiple treatments, including CAR T-cell therapy. Since his diagnosis, this avid marathon runner has participated in several Team In Training events, including the tragic Boston Marathon in 2013.

Dr. Larry retired from active clinical practice and soon after was retained by LLS. Utilizing his clinical and IT experience, he was tasked in leading a program to build a national registry of blood cancer patients, searching for patterns of care to produce better outcomes with less side effects.

Dr. Steven Coutre is a Professor of Medicine at Stanford University Medical Center. His work emphasizes patient care and translational research focusing on hematological malignancies. His research integrates clinical care and novel treatments, primarily for CLL and multiple myeloma.

In this episode of our *Patient-Doctor Perspectives* series, we will be discussing the latest advances and treatments for CLL, the experiences of one patient through multiple treatments, and how CLL patients may fare with COVID-19 and the vaccine.

Welcome Dr. Larry and Dr. Coutre.

Dr. Larry: Yes, glad to be here.

Steven Coutre, MD: Thank you.

Elissa: So, let's start with Dr. Coutre, what got you started in the field of medicine and study in leukemia?

Dr. Coutre: I guess I was always sort of interested in science in general and made a decision to go to medical school at Stanford. And I think there it was just being exposed to different disciplines and being attracted to hematology in particular, and then did my residency, and then came back to Stanford to do a fellowship in hematology and was quickly drawn to clinical research, clinical trials and was fortunate enough to be in an era of amazing discoveries and amazing new drugs. So, it's been an exciting time in many of the hematologic malignancies, the advances that we've made over the years.

Lizette: Doctor, our main focus today is chronic lymphocytic leukemia, or CLL. Could you explain to our listeners what that is?

Dr. Coutre: So CLL it's a cancer of the blood and the bone marrow. If you think of the blood and the bone marrow as an organ system and, you think of lung cancer or kidney cancer, well the blood and the bone marrow is an organ. All of our blood-forming cells are made in the bone marrow, so any of the leukemias, by definition, involve the bone marrow. And this happens to be one that affects our white cells, specifically our lymphocytes. And remember, those are the cells that have to do with our immune system and make antibodies and things like that. And they traffic through our lymph nodes and our spleen; our tonsils are big lymph organs. And so for many patients, those are enlarged also. But that's the way to think of it. We don't think of this the way we do solid tumors where we talk about metastatic disease and things like that.

Edith: That's very interesting, thank you for the great explanation. So, Dr. Larry, you were diagnosed with CLL in 2010. What were the signs and symptoms leading to your diagnosis?

Dr. Larry: As a physician, I'd say to people, "I know enough to be dangerous. I'm not an expert in anything as a family doctor, but I know just a little bit." And back in my days of practice, which started in 1981, I believed, rightly or wrongly, that people should have an annual physical, right. That was women with gynecologic exams, men with regular exams. And so, I did what I believed in, and I used to get a blood panel every year, and I'd see my internist, and we'd have a physical exam.

So, in October of 2009, I had my regular routine blood tests, and I could see by looking at the results that although my total white cell count was normal, it was only like 6,000, and Dr. Coutre would say, "Well you look at that and you say that's normal," I could see that my lymphocyte differential count had gone higher than the neutrophils. And I said, "Wow, that's interesting. Why would that be? Did I pick up a cold or something like that?"

And then I started examining myself, right, and I found some little lymph nodes in my neck that were not really my tonsils. They couldn't have been my tonsils because I had my tonsils out when I was six years old. So, I kind of ruled that out. And I just put two and two together, and I said in October of 2009, "I must have a lymphoma or some kind of leukemia."

Now I kept that a secret from everybody, including my wife, until I went to my doctor for the physical in December of 2009. We talked about it. He said, "Well we ought to do some flow studies to see what you have." And so those were drawn at a visit at the end of 2009. And on January 8th, 2010, I was attending a wedding for my nephew in New York, and I hadn't heard about the flow study yet so I'm like nuts. So, I emailed my doctor, and said, "Well where are the results?"

And so that night on January 8th, he emailed me back and he said, "Well I'm sorry to say you have an atypical form of CLL and probably what's called SLL, which is small cell lymphocytic lymphoma." And so that was it. In essence, I diagnosed myself, and I got freaked out. And he gave me a prognosis based on my flavor of CLL. And Dr. Coutre knows more about this than I do about my genetic mutations.

And at the time because there were no oral targeted therapies or anything, he said, "Well looks like your prognosis is about eight years."

So, I hightailed it to Stanford actually, and I did not see Dr. Coutre in the beginning. I saw a lymphoma specialist named Ranjana Advani. I was suggested to do it because CLL was felt to be actually a lymphoma. I maybe saying that wrong and, Dr. Coutre, you can correct me, but I was sent to the lymphoma clinic. If anybody would've looked at me on paper from my physical at that point, they wouldn't have picked up anything. That's how I figured it out.

Elissa: So, Dr. Coutre, how does something like that happen? How does a CLL patient come in and get the blood test and then get diagnosed with a lymphoma versus CLL?

Dr. Larry: So, what Larry describes is really the classic way that CLL often is diagnosed. Somebody has a blood count for some reason. They notice an increase in the white cells, the lymphocytes. And Larry was more knowledgeable and he noticed a subtle increase. Often, it's, well, okay, fine. Like you said, maybe a viral infection. We'll keep an eye on it. Gets repeated a year later and maybe it's a bit higher, and then they send the test on the blood, that flow cytometry that usually is sufficient to make the diagnosis.

Now a little confusing here between lymphoma and leukemia, right.

So, lots of different lymphomas, and one of which is small lymphocytic lymphoma. But what we've learned over the years is that CLL and SLL are really a spectrum of the same disease, and we really treat SLL just like CLL, not like some of the other lymphomas. But technically you have to have more than 5,000 abnormal cells in the blood for us to call it leukemia, CLL. And if you don't, but you have an increase in your lymph node size perhaps and somebody gets that biopsied and it shows the exact same thing, then we just give it a different name, small lymphocytic lymphoma. At Stanford, we have two different divisions, so, we're a little peculiar, and that's why Larry made his way to the lymphoma clinic originally.

Elissa: So how did he end up with you, Dr. Coutre?

Dr. Coutre: Well, I think maybe Dr. Advani got tired of seeing Larry and said, "I need to send him to somebody else."

Dr. Larry: Well, yeah, I'm a pain in the rear I mean that's what happens, and I ask too many questions. And the truth of the matter actually is that I was fine. I was put on what they call wait and watch protocol. But as a patient, I think most of us call it wait and worry because we're just waiting for the other shoe to drop. I mean just is something going to happen or not? I was in that status for three years. And in 2012, my lymphocyte count had risen up to in the 60,000 level. So, it went from 6,000 and in 2010 went up to 60,000 two years later. And then we noted that it was doubling about every two to three months. And so-

Elissa: Oh wow!

Dr. Larry: -by 2013 even though I was not anemic and my platelets were lower but not tragically lower, my white cell count had made it up to about 120,000, and it was, again, doubling about every two to three months so Dr. Advani said, "Okay, it's time to treat. That's a pattern we want to take care of."

So, I was treated by her for 6 months with chemotherapy. And actually, 11 months after the chemo stopped at one of my local oncology visits, my doctor said, "I'm really sorry to tell you that it looks like you're relapsing, that your cell count has come back." I contacted Dr. Advani and I said, "Look, I know enough to be dangerous and I want to start looking into clinical trials because the regular treatment didn't seem to last very long." And that's when she said, "Well then you need to see our friend Dr. Coutre because he's the one who knows everything about clinical trials and CLL." And so, I don't know what's the correct word. I was either referred, transferred, punted, turfed, or booted into his clinic. And so, I met him in the beginning of 2015 actually and he's been on my rollercoaster now for six and a half years.

Elissa: That's great.

Dr. Larry: He's a master at this.

Elissa: Clinical trials are just so important, especially if you just kind of see, one treatment not working and then what else can we do? So what happened then at that point? Did you go on another treatment? We mentioned in the introduction earlier that you did get CAR T-cell therapy at some point.

Dr. Larry: Right. So, by June of 2015, I was having what's called B-cell symptoms. I was having weight loss, fevers, and night sweats. And I just want to say to the audience that, as a physician, part of my history-taking is always asking somebody if they've had night sweats. I mean that's kind of part of a review of systems. I finally learned what they were in June of 2015. I didn't know what I was asking and then I knew what they were and they're awful. I mean they're just soak the bed terrible.

And so, I had a consultation because I'm a part of The Leukemia & Lymphoma Society family. When I was in New York actually on business, they said I didn't look very well, and I wasn't feeling very well. And they sent me to another CLL specialist in New York who said, "Well you have to be treated." And they had a clinical trial of a drug, although just at that time a drug called ibrutinib became FDA (US Food and Drug Administration) approved Imbruvica®, and so, my choice was to stay in New York for six months or a year and be on a clinical trial or go back home – I live in Sacramento, California – and I could be followed by Dr. Coutre and my local oncologist, and I could get a prescription for ibrutinib, which I did.

And so that was not a clinical trial. Having said that, it worked from June-ish to September-ish. And my white counts came down. I felt better. However, I experienced a bowel obstruction in October of 2015 in my colon. And this was unexpected, and in the end, I was taken off ibrutinib for surgery. The surgery found that a massive lymphoma had obstructed my colon, so I had the right side of my colon taken out with the terminal ileum. And then we were looking for treatments again because it was thought that the ibrutinib didn't work for me, although nobody really knew. I mean it was not anything very clear at all. We couldn't tell if it didn't work, we couldn't tell if it just didn't get into my gut, we just didn't know because everything else seemed to be working pretty well.

Anyway, so in December of 2015, talking to Dr. Coutre, I entered a clinical trial then of a drug called ABT-199, which is now referred to as venetoclax. And I went on that trial, and, again, I'm like an anomaly, okay. So, everybody listening out there don't think that I'm your classic case because I don't think I am and I just am here to keep Dr. Coutre on his toes. That's what I'm here for.

It worked fine, but then by June of 2016, my lymph nodes had grown, especially in my neck, to a remarkably large size. It was clear the venetoclax wasn't keeping my lymphoma component in check. And since venetoclax was a single-arm therapy, and I needed something else, I had to be excused from the clinical trial.

Now at that point in 2016, we talked and thought that maybe CAR T treatment would be good for me at that time. And so, I did sign up for a CAR T trial at Memorial Sloan Kettering in the summer of 2016. And having said that, Dr. Coutre is a very creative fellow, and he knew that I had been on ibrutinib as a prescription drug, and venetoclax was now no longer a clinical trial drug. It had been approved by the FDA and you could get it as a prescription. I was in his clinic, and when I stopped the ibrutinib, I had an extra bottle left, and I brought the bottle unopened to him, and I said, "Maybe somebody could use this. It's really expensive," and I didn't know that once it's prescribed for me, it's got my name on the bottle, you can't hand it to anybody else.

But as I remember the story, Dr. Coutre kept the bottle on his shelf. And at that time in June 2016 when he said, "You know, how about this?" And he walked out and he got the bottle and he handed it to me and said, "Would you mind trying a combination of ibrutinib and venetoclax at the same time?"

"It's not a trial. You'd have to pay for it. We could prescribe it and get it approved through your insurance companies." And we did. Each of my doctors prescribed one of the drugs.

And within two and a half weeks of that combination, everything just dissolved. And so even though I went to Sloan Kettering to have my T-cells extracted and prepared for CAR T infusion, I never used those cells because the combination of those two drugs was like a miracle.

And so, three years, I took that combination of drugs until the summer of 2019 when, again, Dr. Larry doing his own self-exams found nodes again in his neck. And so, it was clear to me that it was coming back and Dr. Coutre agreed, and we decided to do some radiation on my neck just to help my symptoms, because it was kind of bothering me. But PET scans showed I had more nodes in my chest area, which were new. And that's when I was referred for CAR T therapy.

So that's how that all happened, and I had CAR T therapy administered at the Seattle Cancer Care Alliance at the Fred Hutch in Seattle December of 2019. Since December of 2019, I haven't been on any treatments for CLL. I mean I've just been hanging out and we're just waiting, you know, to see how long it lasts. And—

Elissa: Yeah.

Dr. Larry: -that's the whole story.

Elissa: Now you brought up a really good point that I want to touch on with how expensive that medication is. And I'm sure other patients of all different blood cancers can relate to that. How did you get that paid for, because insurances don't necessarily pay for the entire thing?

Dr. Larry: Well, essentially at that time, I was not of Medicare age. I was on a commercial PPO health plan, and the drug companies themselves have copay programs. And I'm not talking about the LLS copay program. I'm talking about drug pharmaceutical company copay programs. And I was accepted into their copay program, so essentially, I had to pay up to my deductible of my private insurance company, and then out-of-pocket maximum on that policy. Well, that's like par for the course today. But having said that, the pharmaceutical companies, each of them who manufactured those drugs offered me a copay card. So, when I went to refill them, the retail price of those drugs would've been about, I don't know, $25,000 a month, and my copay was less than $100 because of these copay drugs.

Elissa: That's great. And you mentioned the LLS copay program. We'll have more about that at the end of the episode, but for CLL, patients can get up to $8,000 in copay assistance. So, if you're interested in that, definitely stay tuned for the end of the episode.

But Dr. Coutre, how have your patients dealt with that in general with just having such expensive medications that are so crucial to their care?

Dr. Coutre: So, Larry brings up a very good point because all of these medications – and you can look across many cancers, and we have all these really remarkable, transformative, innovative drugs, many of which are oral, and they're all expensive. All of them.

So fundamentally, the reason this works is because of the Affordable Care Act.

Elissa: Right.

Dr. Coutre: The Affordable Care Act one of its components is each insurance policy has to have a maximum out-of-pocket per year. And Larry is describing a kind of a classic high deductible plan—where he says, "I'm willing to pay for my $3,600 deductible and even up to $12,000 a year, or whatever it is," because he's insuring himself for a catastrophic event. All it takes is a couple days in the hospital to have a $30,000 bill. So that's what insurance is for, but what about these everyday things?

So fundamentally, what happens is exactly what he described. Normally he would pay his whole upfront deductible and then 20% of the rest until he hit his maximum out of pocket. Except he doesn't, and the manufacturer covers that, and the insurance company picks up what they normally do. So, the insurance company is not paying any more than they would otherwise. It's just that the pharmaceutical company covers his portion of the expense.

Now importantly, by law, they cannot offer that type of program to any government health insurance, ie, Medicare. And Medicare Part D, as you may know, by law does not cover 100% of a drug's cost. Up to 95% which sounds great, doesn't it? Except 5% of a large number is a large number. And so, these are very substantial costs and programs like you describe, The Leukemia & Lymphoma Society and other organizations, really have been a godsend in covering these substantial expenses for many patients.

So that's kind of how things work. It really points out our muddled healthcare system, but, at the end of the day, our obligation is to do whatever we think is best for our individual patient. And we try to make that happen any way we can. And it's not just getting a specific drug. It's all the other aspects of care, financial, psychosocial, all the challenges you face in getting your care that we have to take into consideration.

Dr. Larry: I think the other part because you're asking about clinical trials and I would be not honest if I didn't bring this part up is that clinical trials pay for the drugs on the trial and some of the stuff that goes on, but they certainly don't pay entirely for travel. When I was on the venetoclax trial, and I had to go to Stanford every week for six weeks for three to four days out of the week, it was really not right for me to drive from Sacramento to Palo Alto every day for these visits. I mean the traffic in the Bay Area pre-pandemic was pretty brutal and so we stayed overnight. But the clinical trial did allow a hotel nightly stay budget of $150. And Dr. Coutre, you can't see him, but I can see him smiling on the podcast because everyone knows you cannot find a hotel room in Palo Alto or anywhere close by for $150. This was similar to me when I went up to Seattle for CAR T therapy. The rule is under a CAR T trial that I was on is you had to stay close to the clinic and hospital for 30 days, during the CAR T treatment and post-treatment. And the trial I was on paid no expenses, travel expenses.

There are some financial issues that, really should be talked about when anybody asks about this. And I just want to bring that up. I'm fortunate that I was able to cover high deductible costs and costs of my travel, and otherwise I'm not sure what, I would have done, frankly. But that helped me to survive and that might be a difficult pill to swallow, so to speak, for some people.

Dr. Coutre: Yeah, I think clinical trials really bring out and highlight the disparities that we see in our healthcare system in terms of access to care. Traveling long distances is not trivial. Staying overnights, like Larry brings up, is a huge issue. And although we constantly have the mantra of, participate in a trial, there are real challenges for patients to do this. Hopefully, the pandemic has opened our eyes because of telehealth visits to what's possible. And I think for many of us we're asking ourselves, "Well why were we doing things that way? Do we really need to do things that way?"

I've continued my patients on my trials for CLL with drugs like these even though they're telehealth visits, and it's been perfectly fine. And I hope that when we come out of this, we're allowed some kind of flexibility in routine care and in clinical trials because it's really broadened the availability to get care and to participate in trials by having this kind of flexibility.

Dr. Larry: I agree. The truth is that with the pandemic, after I left Seattle from my CAR T therapy, I've seen my local oncologist once when I returned as the pandemic was just gearing up. And in the last 17 months, the only medical visits I've had are telehealth and the only treatment visits I've had have been for IVIG infusions, which is a side effect of the CAR T. My immune system needs it. And I guess, honestly, I did go up to Seattle at the beginning of this month to have my 18-month checkup. I should've been up there every 3 months, but due to the pandemic, I didn't travel. So, I think the telehealth thing works out very well, and I can say it for myself because I'm going to be self-serving and say I'm a pretty compliant patient, so if something's up, I'll pull the fire alarm. But otherwise, I kind of like it. No offense to not seeing you, Dr. Coutre, exactly-

Dr. Coutre: Yeah.

Dr. Larry: -and shaking your hand which we don't do anymore. It's a very different world. So, I hope we are able to extend these kind of trials.

Lizette: I think it's important to actually make it easier for the patients, right, doctor? We try to do that here. We have clinical trial nurse navigators that actually do a lot of the legwork for patients to be able to go into a trial as well as just trying to help people with finances, like you said, Dr. Larry, just trying to help people with travel assistance, things like that. So, Dr. Coutre, definitely these telehealth visits are really important because you can see someone without having them have to go through all of the logistics while that person may be feeling really ill.

Dr. Coutre: Yeah, it's really been helpful. I think the first thing, of course, is just knowing what's available. I mean how are you to know what new therapies there are or extremely promising therapies that are still in trials that aren’t commercially available? And your local oncologist may not know. They're dealing with a lot of different patients with a lot of different conditions, and they don't necessarily focus in on just one area.

So, getting this information out more broadly is incredibly helpful and then having access to it. And just an initial consultation if we're able to do it remotely, for many patients would be of tremendous benefit. Of course, then you have the challenge where some of the things really do need to be done at a specific center, primarily for safety reasons, but then at least you know what is available and what the potential is. If it really seems something very promising, maybe you're going to do whatever it takes to make that happen for yourself as the patient.

And, of course, with LLS and other organizations we're dependent on you to help with the logistics, to help in many cases with the finances. It's a shame to know that you have something that you believe would benefit a patient, but to run up against these more practical obstacles.

Elissa: Now Dr. Larry, you touched on throughout your treatment and your diagnosis that, you looked at your own blood test results and everything. So, you have said yourself in the past that doctors make the worst patients. So, what was that like for you as a doctor getting diagnosed with cancer?

Dr. Larry: For me, yes, doctors are terrible patients. And I think in my particular case, it's a question of am I interpreting something correctly? And if I am, okay; I don't want to kind of say something wrong, and do I keep a poker face or not to my spouse and family?

It's been kind of an interesting problem because I see things as they come by, and I understand what most of them are. I don't understand what everything is, and I miss certain things.

Frankly, again, from a selfish perspective, I want to know everything. And if I can know things as fast as I can, that helps my mind. Every time I have what's called an MRD test, which is a measurable residual disease which looks for, I call it needles in a haystack. They're tests to look for one in a million cancer cells. And if they don't find any, that's a really good thing. And even if they find a few, that's not so bad. It's just a great way now to monitor our disease.

But I will tell you that, probably for the week before I go get my blood drawn, that's not as bad as the week after my blood is drawn and I'm waiting for the results of the test because I know I can't get them as a physician. I'm not a physician, I'm a patient, and I'm relying on Stanford's clinic, which is very good and they know me, to send me the results, pretty much as soon as they're available.

For me, I understand most of everything. Like I said, I know enough to be dangerous, and I know when I'm comfortable or not. I do think there's a problem a little bit in the fact that health portals today – and I think there's a new regulation but I'm not sure if this is true. Every test that comes out has to be pushed out into the portal whether a clinician has kind of seen it and talked about it with a patient or not. Is that the way it works now?

Dr. Coutre: Yeah, that's right. Each institution is a little bit different policies, but there is some overall rules. But, for example, at Stanford when you talk about routine blood tests, those are released to your portal as soon as they're resulted. It used to be they required the physician to look at it first and then release it, but no more.

But for things like pathology reports, I think there is perhaps up to a seven-day delay. If your physician releases it in one day, then you see it. If they don't look at it for seven days, for example, then it's released to you automatically. So, there's rules like that but you're right, the anxiety associated with waiting for certain test results, particularly biopsy results, particularly patients with cancers, I mean you just you're on pins and needles. And so, we have to continue to refine this process to get that information out to you as soon as possible in a way that you can understand it.

Dr. Larry: Right. That was my point that, personally, I can understand most of what I see, but I do think that the average person who doesn't have a doctorate or a PhD or doesn't know healthcare, all of a sudden, I got a message on my phone from some medical site to say, "You have a result in your folder. Go look at it."

Well, so I go look at it right away. I think most people go look at it right away. And then they're like, "Well what does it mean? What do I do? Who can I talk to?" And so I think it's a mixed bag. I mean everybody wants to know the results, but then everybody doesn't know how to interpret everything.

People know I have CLL, they know I work for LLS and so, they call me Dr. Larry, and I even used to have a website called, *Ask Dr. Larry*, which is not really live anymore. But people call me, or they write me, and they say, "Well what does this mean?" And to a point, I can kind of explain it and I say, "You know, you have to talk to your doctor because I don't want to interpret this right or wrongly." But I think certainly, as a physician, it's helped me get through all this.

On the other hand, it's also a little scary because as a physician, I know what some of this stuff means, and it's telling me that maybe it's not so good. If I didn't know that I might look at results and say, "Oh, they're okay. You know, no big deal." I mean, even though they may be prognostically negative. So it's a mixed bag.

Dr. Coutre: Yeah. I think it really highlights the need to have just a really good and comfortable relationship with your provider that you can trust will let you know when to worry and when not to worry because we can't expect everyone to know everything and all the details about their condition. Some people want to know that, and they can do that, and they do, do that, but many people don't. So, it's really our kind of obligation to guide them and let them know when, gosh, this is really concerning. We really need to do something.

Or a lot of what we do is provide reassurance. And especially with a condition like CLL, the wait and watch or even somebody on treatment, it's communicating that information about a result or about how they're feeling or maybe a symptom that they have when they're taking a therapy whether or not this is something to be worried about. I think that's the bottom line.

Dr. Larry: I also want to say that, obviously, Dr. Coutre is my doctor and he's in Stanford and I'm in Sacramento. But my advice to most everybody who calls me and say, "I've just been diagnosed with CLL," or almost any kind of cancer, frankly, is I tell them that well your doctor at home is probably very good, but in these cases, it's very hard for a general practitioner or even a general oncologist to keep up to date with everything that's going on with that particular cancer. And I recommend strongly, so strongly to everybody that they need to get plugged into an academic center. They need to have a consultation if it's financially viable or travel viable.

Or now, like Dr. Coutre says, with telehealth maybe that's going to make it a lot easier. And it's not just to look over the shoulder of the local oncologist, but it's also for like we're talking about clinical trials that the local folks at home are not as fluent in clinical trials and new drugs coming out and new combinations and new therapies. I hate to say it, but they could be years behind. And in this illness that we're talking about, that could mean a big difference. So, I just want to say that. I think that the Dr. Coutres of the world and his colleagues need to be used. I just think everybody needs to get plugged in with an academic specialist.

Dr. Coutre: It is true. We see a lot of individuals who are coming for more information, whether it be because someone said they need treatment or very commonly because they don't; they're in the watch and wait. And I view us as a resource, right. I mean very busy community oncologists. You're right, Larry, there's just so much that they see. And so we work together, right. We're not here to replace them, but we're a resource. If that patient has seen us, often they get reassurance that what they've been told is accurate, and this is why, and we could provide more detail. And then I'll often say, "Look, if you're concerned that something's changing, if you have some symptoms, you're worried about, if somebody is telling you that you need treatment, that's a great time to reconnect with us and we can look over things." So, it's a good partnership, I think.

Lizette: And there's so many treatments that are available now for CLL and so much emerging treatments. Dr. Coutre, how do you know which treatment to provide to a patient and at what time? Dr. Larry has been through so many treatments. How do you know which treatments are best for a patient and what are you excited about because I know that there's been so many things in CLL that are coming out providing patients with not just better outcomes but also a better quality of life?

Dr. Coutre: So that's a great question. So, there's a couple of things. First, in the watch and wait arena, it stands to reason that perhaps some of those individuals would benefit from earlier treatment and also probably that some would not, once we truly had a curative therapy. But we have started a big national trial to kind of relook at this issue for those at high risk. And that's defined by various features of their disease, again, these are the watch and wait patients, a few additional blood tests, prognostic factors. And if they fall in that category, the trial asks a very simple question. We're going to take a third, and we're going to observe like we normally would, and the other two thirds are going to get treatment with one of our combination regimens for a year. So nice trial for those who are motivated to consider earlier treatment.

Now beyond that, the great thing is we have a lot of choices. And they're all great and they all will work. And I really emphasize that when I'm talking to a patient about treatment choices. And I emphasize that there isn’t a best treatment, which is actually great. There are many best treatments, and they're just different. They range from drugs like ibrutinib or acalabrutinib. There are oral drugs you take daily that we've used indefinitely. I have a couple patients from the very first trial that have been on this for more than a decade now doing extremely well. And now we have time-limited regimens where we combine therapies and give them for a shorter period of time and ask how long is that going to last?

And I think the combination that Larry was on ibrutinib plus venetoclax. We've gotten more and more data about that, some very recent trial results. The CAPTIVATE trial, the GLOW trial were just presented at our very recent meetings in the last month, and I think that combination is likely to get approved as early as next year.

And then the best therapy for a patient is what is best for that patient, taking into account their desires. Do they want to take a pill? Do they want to consider infusions? Are they okay with just staying on a pill that's once a day and quite straightforward? Or are they more attracted to perhaps a little more intensive of a treatment approach but for a limited period of time? And so that gets into that whole dynamic of having that conversation with your patient knowing what they would like and really together making a decision about that particular treatment for them.

Elissa: Now, Dr. Larry, during your blood cancer, you have gotten involved with LLS in multiple ways starting with Team In Training and then moving on to be our Executive Research Director for our National Patient Registry and COVID-19 study. Could you tell us a little bit about that?

Dr. Larry: Yeah. First of all, I want to apologize to Dr. Coutre because on that COVID study we're trying to measure antibody response in blood cancer patients and, unfortunately, we find a lot of people who are finding they don't have much of a response. And then they call their doctor, like Dr. Coutre, and then he gets mad at me because it's like, "Well, what are you studying this for?" It's like, "Of course, everybody on treatment has knocked out their B-cells and what do you expect?" And so, I'm publicly apologizing.

Dr. Coutre: I just give them Larry's cell phone number.

Dr. Larry: Right.

Dr. Coutre: So, it works well for me.

Elissa: Now, you did not get antibodies, correct, Dr. Larry?

Dr. Larry: I did not. And it's a real head game for me. People say, "Well what are you going to do?" And I say, "Well I'm going to keep doing what I was doing. I'm going to wear a mask. I'm going to socially distance." I'm not going to a San Francisco Giant's game, but maybe I'll go to a Cubs game. I mean I don't know because Dr. Coutre and I like the Cubs.

Dr. Coutre: Yes, yeah.

Dr. Larry: But it's just for me a problem. I'm not going to eat indoors in a restaurant. My wife and I still do not go into grocery stores for big shopping. We do eCart; they put it in our trunk and that's how it goes. I did get on airplane to go to Seattle to have my visit. So, I'm just going to be cautiously careful.

Dr. Coutre: So, there's a lot coming along. The data from the LLS will be very interesting because it's a huge number of patients who volunteered to have the testing done. But remember, we don't know that that's the be all and end all of vaccination.

There may be other aspects of the vaccination that provide protection like so-called cellular immunity that isn't measured by an antibody response.

People want to know, "Well what about a booster? Is that going to help?" We don’t know, but there are ongoing studies looking at that getting a third drug and measuring antibodies. Patients, of course, who get organ transplants are on drugs to suppress their immune system, so that's another big issue.

In *The New England Journal*, a very prominent medical journal, there's a very nice study published looking at organ transplant recipients, where they measured antibody responses and before the first dose, of course, zero. Before or after the second dose, I think it was 4%. After the third dose, it was higher, but still quite low. And then they gave everyone a booster.

And it's very interesting. Those who had some antibody response, even though it tended to be low, really had a tremendous antibody response with that third booster and some who had no antibody response after the second shot then had an antibody response. So, it's that kind of information that we need, but, more importantly, we need to understand what these antibody responses and levels actually mean. So don't walk away with the message that if you don't have an antibody response you're not protected but do walk away with the message that Larry just conveyed in that, you still have to be a bit prudent in what you do and your exposure and use some kind of common-sense approaches, including, continuing to wear masks in appropriate situations.

Elissa: Yeah. That's just so tough for blood cancer patients and I can't imagine the emotional impact of hearing that you don't have antibodies. And I know that we're starting to also potentially test T-cells, but then the ones that do have antibodies we don't necessarily know what those numbers mean. I'm an AML survivor. I participated in the study and did have some antibodies, but I don't know what these numbers mean.

So, I don't even know if I'm fully protected. And so, we still need to make sure that we do take these precautions and travel is another thing. It's summer, everybody wants to go out and do all the things and get back to normal life, and it's just so much harder for blood cancer patients not knowing if they are really fully protected.

Dr. Larry: Right. I go through my travel itinerary with Dr. Coutre on every visit that we-

Dr. Coutre: Yes.

Dr. Larry: -have.

Dr. Coutre: Yes.

Dr. Larry: I asked him recently if I could go to Antarctica because, you know, the penguins they don't get COVID and so-

Dr. Coutre: Right.

Dr. Larry: -he actually thought maybe I could. But then I started reading about how to get to Antarctica, and all the ways through Antarctica are through South America pretty much, and South America is just a hotbed of COVID. So, there's no way I'm going to Antarctica because I can't get through South America and then I don't think I want to get on a ship, right, to do the Drake Passage, so that's out. So, we do talk, right, about where I can go and, and, and it's limited right now.

Dr. Coutre: But, you know, going to see the grandkids that's a common one that-

Dr. Larry: Yup.

Dr. Coutre: -comes up. I think, we've gained much more of a comfort level. And it also really highlights the importance of everyone getting vaccinated.

Elissa: Yes.

Dr. Coutre: That's what makes the difference because if the people around you are vaccinated, then you're protected, and the transmission of the virus drops dramatically. We've seen that firsthand here in California, and it's very reassuring. So, I'm cautiously optimistic that as we look ahead in the months ahead, in the next six months, that the story will be a positive one in most areas, but, boy, if you know anyone who's reluctant, encourage them if not for themselves then for, everyone else around them.

Dr. Larry: I think that's the great point. And I think that the word or the definition of herd immunity gets misused. I know of people who say, "I don't need to get a vaccine even though I'm pretty healthy because I'll get taken care of by herd immunity."

Well, the real thing is that herd immunity is meant to protect people who are more vulnerable. And so I want herd immunity. I want everybody to get vaccinated because if every person gets vaccinated, then people like me who are more at risk are going to be safer. Herd immunity is not for people who are healthy and just decide that everyone else is going to protect them and they don't have to get it. Now I'm being selfish, it's for me! And I think that word that gets spread around is misused often.

Now you asked about the Team In Training. Before my diagnosis, I knew nothing about The Leukemia & Lymphoma Society. Absolutely nothing. And when I was diagnosed in 2010, I was an active marathon runner, and I went to my running buddy and I said, "I have leukemia." And he said, "Well you've run every big city marathon except Boston. You have to run the Boston Marathon." The problem was that I'm just not fast enough to qualify, so I went looking for a charity to run for. And I found The Leukemia & Lymphoma Society, because I have leukemia, even though I wasn't being treated.

So, I joined Team In Training to run the Boston Marathon, and my first run was in 2012. And it was great except the temperature at the start was 88° and humid, and so it was my worst marathon ever.

And after the end of that, I said, "I need to go back because it was unfulfilling." So, we went back in 2013, and it was a beautiful day but that was the year of the bombing, and I was stopped four blocks from the finish line. My GPS watch is frozen at 25.86 miles. That's where I was. And a sad part is that I and my wife had raised the most money for the team that year, and so my wife was granted seats in the grandstand at the finish line to watch me come into the finish.

Now my finish would've been right at the time when the bombs went off, so she was in the grandstands at the finish line and watched the bombs go off in real time. And so, I was not able to communicate with her. It took about three hours before she knew that I was okay, and I knew that she was okay. It was a really terrible time. And so that was another unfulfilling marathon for me you see. And the only problem was that that was 2013 and two months later I had to start chemo.

And the end of my story will be when my doctor, Dr. Advani, said, "You need chemo." And I said, "Oh my God! Well, you know, the good news/bad news is I'll start in July, I'll be done in December, I'll have 15 weeks left to train for the marathon again." So, I went through chemo for six months, I trained again, best I could, and I entered the Boston Marathon in 2014, which was a joyous occasion for everybody really. And I wasn't fast, after chemo, but I finished.

Elissa: That's awesome!

Dr. Larry: And since then, that's when I met Dr. Lou, who's now the CEO of LLS, and he offered me a position to build this registry, and the story is continuing.

Edith: That’s truly amazing. So, Dr. Larry, on our patient podcast Home Page, we have a quote that says, "After diagnosis comes hope." Based on your cancer journey and the research experience, what word would you choose to complete that sentence, "After diagnosis comes?"

Dr. Larry: Well, you know, look, after the diagnosis comes dread. That's the word I would use because every patient, including me, enters uncharted waters. I mean it's just dread. Now after the treatment, it's freedom.

It's freedom from being tied down to therapy. It's freedom from not being able to do things that are meaningful and joyous and family related. And COVID ironically for me I was treated with CAR T and I was free, but I was kind of in prison because of COVID. And that to me was the biggest irony of the whole thing that I found a treatment that worked, and I couldn't really do much with it.

Dr. Coutre: So, I would add, after the diagnosis comes dread, followed by hope, by freedom, and by life. Go on living your life. Little bit of a sidetrack with COVID here, but that's going to change. And I mean that's ultimately what you want. You want to go back to normal life in all aspects. And I think over the last decade, these treatments that have come to research, that have come through trials, have come through patients participating in the trials has led to transformation. And, hopefully, a decade from now we'll look back and say, "These drugs are a bit antiquated now." We'll see.

Elissa: I love it. That's really providing hope to any CLL patients listening right now. There are treatments that are working, there's stuff coming in the horizon, and hopefully they can, they can have that bit of hope in the future with getting back to normal and living a life.

Dr. Larry: Thank you.

Dr. Coutre: Absolutely.

Elissa: Well, thank you so much, Dr. Larry and Dr. Coutre, for joining us today. We appreciate Larry telling us all about your story and all the things that you've been through in these past 11 years since you were diagnosed and all that you're doing now, and same with you Dr. Coutre continuing to help blood cancer patients and doing those clinical trials. And we really appreciate both of you for all that you do. Thank you again for joining us.

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. 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.

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 information specific to chronic lymphocytic leukemia at LLS.org/Leukemia.

In this episode, we also mentioned our Copay Assistance Program which can help with out-of-pocket expenses for medications, insurance premiums, and now treatment-related scans and tests. For more information, please visit LLS.org/Copay. All of these links 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.