LEUKEMIA & LYMPHOMA SOCIETY®

THE BLOODLINE WITH LLS

A PODCAST FOR PATIENTS AND CAREGIVERS

Episode: 'Hope on the Horizon: Chronic Lymphocytic Leukemia (CLL)'

Description:

Living with chronic lymphocytic leukemia (CLL) can be a challenging journey for both patients and caregivers.

However, there is a beacon of hope. Tune in to our latest episode, where we speak to Dr. Mayur Narkhede of the University of Alabama about groundbreaking research and innovative treatments for CLL. Discover the potential of CAR T-cell therapy, bispecific antibodies and other cutting-edge options that bring the promise of new hope and possibilities for those affected by CLL. Don't miss this inspiring and informative discussion!

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 Dr. Mayur Narkhede, a hematologist/oncologist and Associate Professor at the University of Alabama. He specializes in the treatment of chronic lymphocytic leukemia, or CLL, Hodgkin lymphoma, and non-Hodgkin lymphoma. Dr. Narkhede is a principal investigator of multiple clinical trials in the development of innovative therapeutic approaches for hematological malignancies.

In recognition of his dedication to research, Dr. Narkhede was awarded the Robert Francisco Award for his work on evaluating a drug in the treatment of side effects following CAR T-cell therapy. Welcome Dr. Narkhede.

Mayur Narkhede, MD: Pleasure to be here.

Elissa: So, our episode today is on chronic lymphocytic leukemia, or CLL. Could you tell our listeners what that is?

Dr. Narkhede: Sure. So, chronic lymphocytic leukemia, or CLL, is a type of non-Hodgkin lymphoma and a cancer of the B lymphocytes of the immune system. It is the most common type of leukemia with roughly about 20,000 cases diagnosed each year.

Lizette: And how is CLL different from other types of leukemia?

Dr. Narkhede: So, leukemia translates to cancer in the blood, and it differs from lymphoma in the sense that it predominantly is detected in blood in most cases. In terms of differentiating CLL from other leukemias, it's chronic, meaning slow growing, lymphocytic, meaning involves the lymphocyte cells of the immune system.

Now compared to acute leukemias, CLL is a very slow growing cancer and not everybody requires treatment and diagnosis, with the majority of our patients being asymptomatic, so that's how it differs from other leukemias.

Elissa: We know that a lot of leukemias and other blood cancers have genetic mutations associated with them. Is that the case with CLL?

Dr. Narkhede: So, CLL does have associated genetic mutations. However, the incidence of mutations vary and these mutations lead to different severity of diseases. The most common mutation that we see is presence of deletion 13q, followed by 11q, and then in a fraction of cases, we see abnormality or deletion of chromosome 17p.

Elissa: Okay. Before we discuss current and emerging treatments, could you tell us what the goal of treatment is for CLL? Is CLL curable, or is the goal more on quality of life for the patient?

Dr. Narkhede: Most of the cases that I see in my clinic are accidentally diagnosed by their primary care doctors during routine blood tests. Most of the patients are asymptomatic. And since it's slow growing in nature, the goal of treatment more so is

to improve quality of life of our patients rather than get to a cure. It's actually considered incurable with our current treatment approaches. And, therefore, the goal focus is on improvement in symptoms, without causing medication-related side effects.

Lizette: That's different than the aggressive forms of leukemia, right, where the goal is different?

Dr. Narkhede: That's right. In aggressive leukemias, the goal is trying to get rid of the cancer completely, improving the quality of life definitely, but also prolonging survival. Since the other leukemias are more aggressive or acute, they tend to be symptomatic very early on and can spiral downwards to bad outcomes very quickly. So, we can't really wait and watch in those kinds of leukemia.

Lizette: Sure. You mentioned that CLL is a non-Hodgkin lymphoma, and I know that a lot of our listeners sometimes say I have CLL/SLL. Can you explain that please?

Dr. Narkhede: Yes, that's a very unfortunate name for the disease where there's a lymphoma and a leukemia component both in the name. This dates back to the time when we didn't have sophisticated technologies to identify cancer cells in the blood; and we used regular complete blood count or CBC to diagnose patients.

CLL means you need to have certain number of circulating cancer cells in the blood, and that number was more than 5,000 in the past. If you did not have that number, but you had enlarged lymph nodes, and the biopsy of the lymph nodes showed that you had the cancerous cells in the lymph nodes only, then it's purely SLL, or small lymphocytic lymphoma, because the cancer has not yet traditionally spilled out into the blood.

Nowadays our technologies have advanced significantly, so we are able to detect very small number of cancer cells. So, a pure SLL is extremely rare to find, though we do occasionally see patients with no circulating cancer cells in their blood but enlarged lymph nodes, which, when we biopsy, shows those SLL cells. So, that's the difference

between them. But in terms of prognosis, treatment, everything else is exactly the same.

Lizette: Thank you. And, what are the current treatments for CLL at this point?

Dr. Narkhede: The treatment of CLL is very patient centered, and it's dependent on the age of the patient, comorbidities, medical conditions, and also genetic mutations in the CLL cells that we talked about a few seconds ago.

So, after diagnosis, if a patient is asymptomatic, with no other symptoms with a normal blood count other than elevated white blood cells, we go to a period called wait and watch. What this means is this includes an observation of how the cancer is going to progress. When we say observation, it's an observation of blood counts, as well as you as a patient where we monitor your symptoms. We ask you follow-up questions every three months ideally for the first two years. And then later on, as we get a sense of how the disease is progressing over a couple of years, the visits can be spaced out to every six months. So, in this wait and watch period, we are trying to closely monitor and identify if we need to start treatment early. If we don't, then we let it be and we let you enjoy your life.

Lizette: A lot of our patients call it watch and worry, right?

Dr. Narkhede: Yes, the watch and worry phase has been very popularized. It is truly very anxiety provoking. If I was a patient and I've been told I have cancer, the C word really scares me. But, when the doctor says, "Well, we don't have to do anything about it," I would be worried, scared, anxious, as well.

But we have to understand that sometimes treating the cancer is not necessarily good because our treatments itself can really cause a lot of side effects. So, we have to balance what's good for you in the long term and what's going to treat the cancer, if it's going to make you live longer.

Elissa: But we also like to refer to it as active monitoring, as it still is a treatment itself, even though they're not getting medications or something else, correct?

Dr. Narkhede: Absolutely. That's why I included it in the category of treatment. Wait and watch, active monitoring, this is not something where we are going to let this be handled by your primary care doctor. You will still be seeing a hematologist or a medical oncologist who specializes in cancer treatment. What we are looking for is signs that we can pick up early so we can start treatment sooner, rather than waiting for too long before things get out of control.

Lizette: Sure. And, what are the other treatments?

Dr. Narkhede: So, we just determine treatments based on certain things. You need to have symptoms, and the symptoms that we define are called B symptoms. And B symptoms include significant weight loss, which is 10% or more of your body weight in six months; drenching night sweats that require you to either take a shower or change your clothes, which usually only occurs at nighttime; or lymph nodes that are causing difficulty in either shaving, moving your neck, swallowing, or if you have enlarged lymph nodes in your groin, and you have difficulty walking, that's a reason to start treatment.

When we focus about what treatment to use, there are actually two major paths to follow; and here's where a patient-centric approach really plays into the center stage.

There are two main pathways. The first one's something called fixed-duration therapy. This is where we use a combination of an injection or infusional medicine. This is a monoclonal antibody called Gazyva®. This is given every month for six months. And then on top of that, we use a pill called Venclexta® for a period of 12 months. This treatment requires close monitoring, multiple follow-ups to the clinic. There might be a period of hospital admission for a patient. So, it's a little bit more involved.

So, there's a second pathway for patients that can't make it to the hospital or don't like to be monitored that frequently, and that's with something called BTK inhibitors. These are pills which target a specific enzyme in the cancer and prevents it from growing. There are three types of BTK inhibitors; and that's, your physician will choose what's the best, depending on your medical history.

The treatment with this type of therapy is often indefinite, meaning we keep you on the treatment till either the CLL worsens, or you develop side effects. And this can be years of treatment, unlike Option 1 where it's only one year of treatment. This is the frontline treatment.

Now, if your CLL comes back, unfortunately, or it progresses or whichever option that you chose, we switch around. So, what option we did not use, we use the other one. That's usually your second-line treatment option.

And then third line or later, we do have newer drugs and therapies that have recently been approved by the FDA. One of them includes CAR T-cell therapy, which is a promising option. However, it's still not considered cure in CLL like it is with other lymphomas.

Elissa: Could you explain CAR T-cell therapy to listeners who may not know?

Dr. Narkhede: Yes, of course. So, CAR T-cell therapy, it's

chimeric antigen receptor T-cell therapy, which is produced from your own blood cells. It's a two-step process where we first take your cells, genetically reprogram them so that they can specifically target your cancer cells. And then we give it back to you as a separate infusion.

As you can see, this involves two steps, so it takes about, on an average, six weeks to eight weeks from the time you make a decision to actually get the treatment. This is boosted immune cells, so the hope is one infusion is done and then the CAR T cells, all your immune system cells will multiply in your body and kill the cancer as it's there.

So, it's a one-time live therapy. The hope is that it may be able to cure a few patients. We are yet to see that in CLL.

Elissa: Is there a reason for that, that you haven't seen that yet with CAR T-cell therapy?

Dr. Narkhede: The reason lies with the fact that we tend to use CAR T cell more in a relapsed setting where patients have usually seen multiple lines of chemotherapy. Some of these chemotherapies damage your immune system, especially the T cells. And as you can imagine, the CAR T cell is heavily dependent on your immune system. So, if you damage them with chemotherapy and then try to increase their effectiveness, you get a poor-quality immune system that you're trying to use to kill the CLL. That's one of the main reasons we think that we are not able to cure CLL with CAR T-cell therapies.

Elissa: Do you think that it could be moved further up the line potentially to a first- or second-line treatment?

Dr. Narkhede: There is a possibility that that will happen in the near future. The challenges lie with the fact that this is a very expensive therapy, also the logistical concerns regarding who can administer CAR T. Not every doctor's office can administer CAR T. It is a more specialized treatment and select CAR T centers can only administer them. So, these two barriers need to be overcome rather before we can use CAR T cells for everybody.

Lizette: Now, are you looking at CAR T more so than stem cell transplantation for CLL patients?

Dr. Narkhede: That's right. The outlook in the field has shifted towards using CAR T rather than stem cell transplant; and the reason being, the kind of stem cell transplant that we use is called allogeneic stem cell transplant or we use somebody else's immune system to fight the cancer.

When we do this, we run into problems of significant side effects and toxicity, in addition to finding the right donor, which can take months. The side effects are extremely high, and about 30% of the patients can actually die just from the treatments, versus the mortality of dying from CAR T is extremely low.

Lizette: Okay, and I know that we are now hearing more about bispecifics [antibodies]. Are bispecifics appropriate treatment for CLL patients?

Dr. Narkhede: Bispecifics, as of right now, are still in clinical trials; and we don't have any available bispecifics to be used in the clinic. They are an interesting concept where we are trying to enhance the effectiveness of antibody therapy by using a dual antibody with one arm that'll attach to the CLL cells and the other arm that attaches to your T cells.

So, as you can imagine, you need to have a healthy T cell for this therapy to work. Right now, it's still very early to say if this is going to be approved, if we are going to see good responses from this that are lasting. The initial look at it appears that there are responses in patients, but there are some challenges with this therapy. Unlike CAR T cell, this is a multiple infusion indefinite therapy versus CAR T was once only. This needs to be given, ideally, every week or every few weeks. And the data for using or stopping early is currently unclear.

Elissa: We'd now like to take a short break to hear from the LLS Financial Assistance team on copay assistance for patients with CLL and other blood cancers. We'll be right back in just a moment to discuss side effects of CLL therapies with Dr. Narkhede.

What are the side effects that CLL patients can expect either from the disease itself or from treatment? And are these side effects manageable?

Dr. Narkhede: Yes, so the side effects that worry me the most in my CLL patients, and I often tell my patients is infection is your biggest enemy. Not only are patients with CLL immunosuppressed, when we decide on starting treatment, the treatment

further reduces their immune system and increases their risk of infections. Most of the bad things that happen with patients during CLL treatments, usually revolve around pneumonia, UTIs (urinary tract infections), and infections. So, infections is a big one.

Then there are definitely a few drug-specific side effects, such as BTK inhibitors increase your risk of bleeding, bruising, increases your blood pressure. And some of them do increase your risk of atrial fibrillation or a fast heart rhythm.

The other medication I spoke about, the Venclexta, actually does its job as an anticancer medicine too effectively, so that it kills a lot of cancer cells, and that can actually be a problem from the acid that's released from the dying CLL cells called uric acid. So, managing the side effect which is called tumor lysis syndrome can require multiple blood tests every week or even a hospital admission.

Other than infections, in terms of managing side effects, depend on what particular side effects an individual patient's experiencing. We can either stop the drug completely, give you a drug holiday, reduce the dose. To help you with the uric acid that is released with the Venclexta, we usually start treatments with acid-suppressing medicines like acyclovir, give IV fluids. And for infection risks, sometimes we notice that some patients have much more frequent sinus infections, or they have pneumonias that lead to hospital visits. And when we check their blood, they have low IgG. So, these patients do benefit from periodic IVIG infusions to reduce the infection burden.

Most of the side effects cannot be predictable and very specific to the patient. So, it depends on how an individual is fairing and modification to therapy may be needed.

Lizette: I know that sometimes patients don't want to let you know that they're having side effects, particularly if the medication is working against their disease. They think that maybe you'll take away the medication that's working or something else will happen. Do you speak to patients regularly asking about side effects and letting them know that there is something that could be done?

Dr. Narkhede: Yes, so, I think this is very important in follow-up where we have a more focused history-taking about symptoms rather than asking how they're doing, because absolutely, patients are worried that if they tell me about joint pains, I'm going to take their medicine away. They might be okay with their joint pain, but they would not be okay with not taking the medicine.

So, before I make decisions about stopping treatment, one question I ask them is, "Is this something you can live with, or do you want us to make any changes to your medicine?" And most of the time if it's a minor symptom, they don't bother; and they say they can live with this.

Then the next question is, how are we going to manage the side effect? If it's something they can live with, I'm okay continuing the same medicine at the same dose. But if it's a side effect that significantly changed the person, for example, if they are experiencing shortness of breath, and I know it's from the medication, I'm not going to keep going even though my patient would say he wants to continue because there are certain risks with it. However, we are also not going to stop the treatment completely.

So, what we do is drug holidays and reducing the doses of the drug. So, my constant message to my patients is please be clear with what symptoms you're experiencing. It's not that I am going to stop your medication right away. Everything is a discussion. We will give you a holiday. We'll give you medication to manage the side effect. Our goal should be aligned, where we want to get rid of as many CLL cells as possible. But at the same time, not being very bothersome or dangerous to you in terms of symptoms.

Lizette: Yeah. I know that we've been talking about CLL being a chronic disease, so after that wait and watch, patients are pretty much waiting to see when the disease is going to progress and that could be, as you mentioned, hard on patients and anxiety

producing. How are you working with patients on the emotional impact of having this chronic disease?

Dr. Narkhede: It's tough. There's no right answer to this. It depends on how anxious an individual person is, how much help they need.

I do mention to my patients that things do get better as time moves on. I mean, at initial diagnosis, everything sounds scary, everything is new. But as we talk through it, I do an exam. I usually ask them to feel the lumps that I feel by themselves. So, they get a sense of how big their lumps are, and then they can track those lumps at home by themselves.

After the initial visit, I usually, if I feel somebody's very worried about their cancer, I ask them to come back within a month so that we can sit down and debrief and see how the month went and how everything is.

Over a period of time, as time progresses and people get comfortable with monitoring their symptoms, tracking their symptoms, tracking those lumps that we talked about, they notice that the lumps actually get smaller with time sometimes, and sometimes they get bigger. But they can still continue what they're doing. Their anxiety usually gets a little better.

There are also times I feel that I need help, and this is where our wonderful supportive care colleagues where I work come into play. We have trained cancer psychologists who can talk to patients and help them cope with their diagnosis, not necessarily with medications, always. But if needed, they can help with medications as well and refer to a psychiatrist. But I do use supportive care services if needed.

Elissa: That's very good to know.

Now, let's discuss the future of CLL treatment. Are there any emerging therapies or those on the horizon that you're particularly excited about?

Dr. Narkhede: There are mainly two therapies that I'm very excited about. One of them is a newer type of drug. It's called a BTK degrader. Like I mentioned before, currently we use BTK inhibitors. So, instead of inhibiting the enzyme, this medicine completely destroys or degrades the enzyme-

Elissa: Wow.

Dr. Narkhede: -which is what causes the CLL to progress in the first place.

They are very promising. I think there are a couple of products that are being developed in clinical trials; and we will hear more and more about them in the treatment of CLL.

The other one is bispecific antibodies that we very briefly alluded to. These are versions of CAR T which are given more frequently but still depend on your T cells. And now eventually in the future, we will find a way to either augment the patient's immune T cells or maybe have a CAR T cell that is completely made from a healthy donor such as a pluripotent stem cell. This is basically a petri dish of stem cells that we can collect cells from and then manufacture the CAR T. These will be called allogeneic CAR T cells.

These CAR T-cells, we hope, will have benefits of both. First, by using a very young and healthy T cell, we might be able to get rid of almost all CLL cells; and we may be able to use the word cure in these patients. But also, these are modified in such a way that these external cells don't attack their own body, so we don't get those bad side effects that I mentioned that you get with allogeneic stem cell transplant.

We are still yet to see any successful product to be developed, but I think that's something that's on the horizon that will change the treatment landscape for CLL.

Elissa: Wow. Is the concern with allogeneic CAR T-cell similar to the concern with allogeneic stem cell transplant as in, you might get GVHD or graft-versus-host disease?

Dr. Narkhede: Not really. That's the modification that they're making in the allogeneic CAR T cells. In the allogeneic CAR T cells, they're making changes such that the T cells don't recognize your body cells. If they can't recognize your body cells, then they can't react to it, and they don't destroy it. So, you don't get the graft-versus-host disease; but they will still have normal receptors where they can detect the cancer cells. So that's the advancement in the field about this.

Elissa: Okay. Now, our final question for you today, 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 CLL?

Dr. Narkhede: My statement that I often quote, or often say for patients with CLL is many people on the street are walking with this disease. They just don't know it yet. You know it because you went to the doctor to get your blood tested, and I think that's something that helps them understand the scope of what we're talking about, that this is an asymptomatic disease.

The other thing I tell them is new treatments are often on the horizon. I just mentioned two right now, and this might be standard of care in the next couple years. Because this is a very slow-growing disease, we have multiple options right now; and newer and newer treatments are being developed, especially thanks to LLS and other research organizations that fund them.

But by the time you're going to need next line of treatment, there will be more options that you will have. So, it's like putting you in a time capsule and just seeing what's going to be up there in the next few years; and then maybe we will reach to a point where you might find a treatment that can even cure your CLL. And I think that's the hope part of it, that there's always going to be something in the horizon that's going to target your CLL.

Elissa: I love that, and that is so, so important for patients and their loved ones to understand that blood cancer research is ongoing. There are so many new treatments

coming out all the time for different blood cancers, and so it's exciting to see where this might go in the future for CLL patients.

So, thank you so much, Dr. Narkhede, for joining us today. We really appreciate you talking all about CLL and certainly, I think, giving hope to patients. So, thank you, again, for being here with us.

Dr. Narkhede: It was my pleasure to be here. Thank you for having me.

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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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.

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