

## THE BLOODLINE WITH LLS

A PODCAST FOR PATIENTS AND CAREGIVERS

### ***Episode: 'CTCL: Skin Lymphoma, Not Skin Cancer'***

#### **Description:**

In its early stages, cutaneous t-cell lymphoma (CTCL) may be mistaken for a skin condition like eczema. Many people have a hard time grasping how something that arises in the skin is actually considered a blood cancer. Listen in as Alicia and Lizette from The Leukemia & Lymphoma Society (LLS) speak with Dr. Jasmine Zain, hematologist/oncologist at City of Hope in Duarte, CA, about how CTCL is not just one disease, how CTCL is diagnosed and treated, why dermatologists may be part of a person's treatment team, the prevalence of CTCL within certain geographies and ethnicities, stem cell transplants, the role of clinical trials and the importance of a team approach when determining the best treatment options. Dr. Jasmine Zain also explains how people can live their normal lives despite their CTCL diagnosis.

#### **Transcript:**

**Alicia:** Thank you for joining us on this episode of the Bloodline with LLS. I am Alicia.

**Lizette:** And I am Lizette. Thank you so much for joining us on this episode.

**Alicia:** Today, we will be joined by Dr. Jasmine Zain, hematologist/oncologist, at City of Hope in Duarte, CA. For those who may not be familiar with you, Dr. Zain, would you mind introducing yourself to our audience and telling us what brought you to the field of medicine; specifically, hematology/oncology?

**Dr. Zain:** My name is Jasmine Zain. I work at City of Hope in Duarte, CA as a hematologist and transplant physician and, basically, I have been doing this almost 25 years now. I have been doing lymphoma therapies for about 20 years so I am very familiar with this area. I actually got into taking care of patients with CTCL very early in my career. I had just finished my fellowship and started my first job at the University of Connecticut, where they wanted to set up a CTCL clinic, a multi-disciplinary clinic that we will be talking about later in this episode, where a dermatologist and a hematologist work together to take care of patients with skin lymphomas. I was very green—didn't know anything much about this other than what I had learned in fellowship; and I said, "yes". Usually these things fall to the junior-most person and that was kind of the start of this really long and wonderful journey. And, I have just continued to have opportunities wherever I worked to take care of these patients. And, now we have an excellent clinic at City of Hope where we see patients together with dermatology and, sometimes, our radiation oncology colleagues.

We review the pathology slides. We see patients from early stage disease to really late stages and I also take care of these patients when they go through transplant. It's really a wonderful experience and I am privileged to be part of this team and to take care of these patients.

**Alicia:** That is awesome.

**Lizette:** Do you just want to give us a sense of what cutaneous t-cell lymphoma is to maybe some listeners that are not familiar with this disease?

**Dr. Zain:** Sure. So cutaneous t-cell lymphoma is basically—it's lymphoma that arises in the skin; and, just for clarification, I want to say it out very clear. Lymphoma is a cancer. It is a cancer of the blood type-- It is a blood cancer that arises, generally, in either our lymph nodes or bone marrow, but it can arise in any organ because lymphocytes basically circulate in our blood and they are our first line of defense providing immunity for us against different viruses and other foreign insults. So, these are an important part of our immune system and they live everywhere. And so, essentially, this cancer can arise in any organ; the most will arise in lymph nodes and blood organs, like liver, spleen and bone marrow. Skin happens to be one our largest lymphoid organs because it is our first line of defense and, if you look at the skin under the microscope, you will see lymphocytes sort of at the edge of our skin. And if they become malignant, they will manifest themselves as lymphoma of the skin and the patients will have skin lesions rather than enlarged lymph nodes or other manifestations of lymphoma. It is important to understand that skin lymphoma is not skin cancer and it is very different than the common types of—you know it is a different disease compared to, say, melanoma, or other types of skin cancers that arise in the skin, but from skin tissue, from skin cells. That is the main difference. The other sort of main difference between skin lymphoma and systemic lymphoma are not as, you know, I called the lymphomas that arise in other parts of the body, is that cutaneous lymphomas will arise in the skin and, for the most part, they will stay in the skin, which makes them unique. Very rarely do we have patients with cutaneous lymphomas who actually have systemic involvement of other organs. Sometimes you will have lymph node involvement, but other than that, it is very rare to find patients with a disease that is in the lungs, or liver, or kidneys; and these are usually cases that are very advanced or they have changed or transformed into more aggressive forms. But the more common forms of cutaneous T-cell lymphoma tend to remain in the skin.

Also, it is important to remember that cutaneous t-cell lymphoma is not one disease. There are many different sub-types, out of which mycosis fungoides is probably the most common, but you have other sub-types as well, including some certain types of b-cell lymphomas.

Cutaneous lymphomas generally tend to be of t-cell sub-type. That is why they are called CTCL, but I think they should really be called cutaneous lymphomas, out of

which T-cells are actually the most common, but you can also have b-cell lymphomas of the skin—that arise in the skin and, again, stay in the skin.

Another sort of interesting point to know is that systemic lymphomas—the most common sub-types are b-cell sub-types (“b” as in boy), whereas in skin, it is actually reversed. The more common sub-types are t-cells (“t” as in Tom), rather than the b-cells. That is another sort of unique feature of these cutaneous lymphomas that we need to be aware of.

**Alicia:** You said that CTCL describes many different disorders with various symptoms, outcomes and treatment considerations. How is someone diagnosed with CTCL?

**Dr. Zain:** So CTCL—remember so now we are talking about t-cell lymphomas arising in the skin and we should also clarify that sometimes b-cell lymphomas will also present the same way in the skin. If it is CTCL, it will mostly present itself as a skin lesion (a rash)—redness, itching, maybe a bump. Most patients don’t pay—you know—they are very small and they are also in areas that are not exposed to the sun, so they are hidden. Most of the time, you don’t see them and the patient may not be aware of them. Eventually, they will start itching or they will seek attention and the initial diagnosis are usually that it is an eczema; it’s psoriasis; it’s an allergic reaction to something. That is how sort of benign-looking they can be or how common—they look very similar to other common skin lesions. There are some patients who present with more aggressive forms where the lesions are more sort of scary-looking, for lack of a better word. They may be tumors. They may be ulcers. These patients will have a slightly more aggressive course. Obviously, they will seek medical attention a lot faster because they will be concerned about this thing that has popped up on any part of their skin. It may be painful. It may be ulcerated and oozing so there are different manifestations. There are also situations where a patient may actually have lymphomas inside their body; a systemic lymphoma where they start to have skin lesions, like a metastatic-sort of situation. We are not talking about those situations at the present time. Those patients will have a very different clinical outcome and they will be treated for their systemic disease and that will take care of those skin lesions. But for cutaneous lymphomas, it is mostly a skin lesion that pops up and that is one of the reasons why diagnosis is so difficult; especially in early stages, because it looks for all the world like anything—a bug bite maybe, or an allergic reaction. And even to an expert, a dermatologist, on this, you do a biopsy or start thinking of something more sinister. They would usually not think of CTCL as the first diagnosis.

Another thing to remember is that it is not, fortunately, not a common disease. It is a rare disease. We don’t see a lot of cases. It is a very small percentage of overall lymphoma incidents so it is not something that most people think about, whereas skin rashes are very common; so common things first. People will generally treat them as a common skin problem. What I tell patients, it is not wrong if your dermatologist misses it for the first time. They’re not, you know, it doesn’t reflect that they are

incompetent or anything. They are doing their job. The important thing is that if the lesion does not get better. Obviously, if this is cancer or lymphoma, it is not going to get better with just--or it will keep coming back; and that should be the cue that there is something wrong; something more needs to be done; and it needs more attention. And, at that point, maybe consider a biopsy or go see a different specialist and, even if they are a dermatologist, they probably start thinking that maybe something else should be part of--the differential should be that's when they really start thinking that this may be a more you know a different thing, or maybe a CTCL; and they would start thinking about biopsy and looking for signs and symptoms of this other disease.

**Lizette:** Sure. And do some people stay with their dermatologist for treatment or do most people get treatment from the hematologist/oncologist since it is lymphoma, a blood cancer?

**Dr. Zain:** That is a great question. It really varies. It really varies with the expertise that you have available at that time. So, in terms of experts in cutaneous t-cell lymphoma, we certainly have dermatologists who are experts, who basically focus and have spent their lives looking and thinking about this disease and treating patients, and they would definitely be part of the treatment team. And, I know dermatologists who treat almost all stages of the disease unless patients require chemotherapy. On the other hand, there are hematologists/oncologist, there may be a situation where the patient gets reported to them very early in the disease course because the dermatologist says, "it's lymphoma, you know I don't want to deal with this. Go and take care, you know go to a hematologist/oncologist." What we need to remember is that—what we need to realize is that this really is a very special disease and it really kind of straddles both disciplines of dermatology and hematology/oncology; and we really need to find the right expert. It doesn't have to be the right specialist. It does have to be the right expert who knows this disease. We don't, certainly, don't want to send our patients to an oncologist, who is going to start giving them chemotherapy, thinking, "Oh lymphoma; let's give them the most common chemotherapy for lymphoma." Certainly, not the case because these diseases can be treated with skin-directed therapy for many, many years before the patient needs anything systemic, intravenous, or even oral. And, certainly, long before they need any kind of chemotherapy which, again, for a trained hematologist/oncologist is very hard to accept because we are trained to treat these conditions with aggressive chemotherapy. That's our job; and, again, this being a rare disease, most people will treat the common things first so we need to make sure that the oncologist understands that this not to be treated like systemic lymphoma; that they need to collaborate with their dermatology colleagues to make sure that the patients have the benefit of the dermatologist's expertise, as well.

Secondly, what we need to understand is that these are skin lesions and there is skin involvement and there is skin care that can help the patient, which, again, I, as a—if I wasn't working in this field, I wouldn't know; I mean I wouldn't know how to prescribe

the right moisturizer or how to take care of their itching, or how to take care of some of the skin issues that arise, wounds, for example, so it is always good to have a collaboration. In each community, I think it's—for the patients to try to find a center that treats these conditions rather than a specific dermatologist or oncologist. And this is a plug for the Cutaneous Lymphoma Foundation, which has been wonderful in supporting these patients and in supporting us as well in our work. They could help you find the right place, wherever you are in the country, or the world for that matter.

**Alicia:** So, it is something we found interesting. Here at the LLS, we have something known as the LLS community and what it is—it is an online platform for patients to speak with each other in order to get support, get information, you know in regards to their own diagnosis. Now, we usually post a question of the day, ...

**Dr. Zain:** Okay.

**Alicia:** And one question that we asked, you know the users who had or who was diagnosed with CCTL? And we found that those, out of the 12 who entered their race, 3 patients or 25%, were African-Americans; and that was compared to the 4.8% of community members—of course, those who voluntarily disclosed their race who were African-American. So to kind of further follow that thought, we were thinking, “okay, let's see the incident rate”. Let's see where this kind of presents itself and, in an abstract on NCDI.gov regarding demographic patterns of CCTL incidences, it explained that while CCTL primarily affects Caucasian individuals older than 55-years-old, it confirmed that it presents at a younger age with more advanced disease stages in African-American and Hispanic individuals. We found that to be extremely interesting. Is there more research on that or is there a reason for that?

**Dr. Zain:** I can't tell you if there is a specific reason. There are some theories about it. First of all, darker skin individuals may not see the rashes as easily. A red rash, an erythema, certainly is more prominent on fair skin. That may be one very simple reason why lesions, by the time they become—and they are not always itchy—so become symptomatic or somebody once seeks attention that they have a more advanced stage, but that may be a very simplistic explanation. The other explanation may have to do with disease biology that we are trying to look into to see what are the differences in the patients—different patient's diseases; and certainly, we are now in the era of genetic testing and genetic sequencing; and I am sure that this kind of information can help us figure out what leads to the cause of this disease. First of all, we don't know what causes it, and that there may be certain environmental factors or other things that we will eventually learn about that may contributing to the onset of this disease; and it may also explain these racial differences. Certainly, we find racial differences in other types of cancers and lymphomas as well, so there is certainly a biologic basis for this as well. What I find in our practice is, certainly, patients who come to us who are African-Americans, for example, have more some of the more aggressive forms of the disease. They have what is called follicular tropism mf, for

example, I find that to be more—just kind of—I can't say actual numbers, but just, in fact, it seems to be more common, and that tends to have a more aggressive course. Now, remember, we are a specialty center so I don't think what we see at the City of Hope is reflective of what the community sees so we will see patients who have been referred to us. So that may be one of the reasons we are seeing more aggressive disease and then that tends to be somewhat—you know, I don't think that reflects the racial differences in the community of the incidence of this disease, but yes; I have heard of that. I also know that patients, African-American patients particularly, have a worse prognosis. Again, I have actually seen that. They tend to have—they seem to have a higher percentage of patients who will have a more aggressive course because there is a small percentage of patients with CTCL who actually have a very aggressive course, which can be lethal within a few years of diagnosis. They just progress very quickly. Even the skin, they tend to have more transformed disease and then it gets into their system, into their organs and, obviously, then it's a different game. And we have had some very aggressive—have seen some very aggressive courses in young patients who are non-Caucasians. I wish I had a better explanation than that, we are looking into that.

**Lizette:** Yeah. It is also interesting, then, in the United States, there is not a lot of young people diagnosed with cutaneous lymphoma. They say, like 5% maybe, before the age of 20, but in other countries; in other parts of the world, there are a lot more patients that are children with this disease.

**Dr. Zain:** So, we do know that it arises out of—possibly arises out of a setting of inflammation and, certainly, when you look at the biopsies of patients with cutaneous lymphoma, you see evidence of a lot of inflammation. So, psoriasis, for example, also precedes a lot of these patients so maybe there are some environmental factors that may contributing to these differences.

**Lizette:** And we really don't know the cause of cutaneous t-cell lymphoma.

**Dr. Zain:** No, we don't. No. People have looked into viruses, infections, you know again, inflammation. There is no real consistent findings that can explain any of this.

**Alicia:** And jumping back to a treatment and kind of seeking centers for treatment, what are the available treatment options for CTCL patients and what is the goal of treatment for CTCL?

**Dr. Zain:** The goal of the treatment is control of disease. So, I wish I could say the goal of treatment would be cure. Unfortunately, we don't have curative treatments yet and by "cure" I mean—so that usually scares patients right away. "Oh, you are not going to cure me. I am going die." So, I--you need to take a pause back and think about this. The cure means really something that is going to treat the disease at whatever time period and then it never comes back. In my mind, that is cure. And

there is a lot of diseases we treat that we don't cure; for example, diabetes, heart disease. So, if you think of it in those terms, we actually have a lot of treatments for cutaneous lymphomas; and I always reassure patients that 90% of the time they will have a normal life. It's not going to affect their life expectancy. They will need treatment, though, for the most part of their life. There may be times when the disease becomes—goes into remission, is very quiet, but most of the time, they will need some kind of treatment. With this approach, we then have to think about how to start treating these patients and how to maintain treating them for the rest of their life so we don't want to run out of all our options right away. So, think of a tool bag. You have maybe 20 tools in it so you want to pick the right tool for the right time, but not—try to keep the big ones for later on. As I said, there are patients who have an aggressive course and they are, again, a small percentage; I would say about 10-15%. And there are also patients who will slowly progress into a more aggressive stage. So, that aggressive stage can happen early or late. Again, factors that determine that are still unclear. In those cases, we need aggressive therapy. For the most part, though, we can start with very simple skin-directed treatments like treatment, for example, topical treatments and that can certainly take care of their skin lesions for a long time. They may not completely clear, but if their symptoms of itching, or discomfort, or disfiguration get better, I think that is a reasonable goal for therapy at the present time. We are hoping that we will have better treatments that we can actually tell patients, "we are going to cure you"; and, certainly, there is a lot of research into that, but for the moment, the treatments are what I call palliative and can get most patients into remission or clear their disease, since it's skin disease. We don't need scans or anything. We just look at their skin and see if they are doing better or not; and that can buy a lot of time. And then, also, even systemic treatments are non-chemotherapy-based. A lot of systemic treatments that are even approved by the FDA; for example, one of the common drugs is Targretin, which is a retinoid, a vitamin A derivative, and has excellent response rates in CTCL. Things like interferon, which is an immune modulatory agent. There are things, sort of non-chemotherapy-based biologic agents that can help treat this disease for a long time and, eventually, most patients will require, if it is progressive, they will require IV or systemic therapies. And chemotherapy and stem cell transplant is really for a very small percentage of patients, who either have transformed disease, or meaning that it has become more aggressive—biologically it has become from an indolence low-growing disease to a more aggressive disease or, if they have developed metastasis. Again, a small group—a small percentage of patients. So, that is kind of the overview of therapies for CTCL.

**Lizette:** And the transplant, would that be a transplant from their own cells or from a donor?

**Dr. Zain:** It has to be from a donor. We have tried doing transplants from their own cells and we found that it doesn't work. Most patients relapse pretty quickly. So, in certain groups of patients, a transplant from a donor has been curative, so that is a curative therapy, but it comes at a big cost. A donor transplant can be toxic. You

require immune suppression. It has a lot of side effects and disease-modifying effects, I would say, because your quality of life can be vastly affected by that kind of transplant. So, we do not try—we don't try to do that in most patients, if we can avoid it.

**Lizette:** Sure.

**Alicia:** I know we always educate our patients and caregivers, or our entire audience on clinical trials...

**Dr. Zain:** Sure.

**Alicia:** That is something that you know usually when you ask somebody, "what are the 3 words that come to mind?" They say, "placebo", or you know "guinea pig", or "last resort.

**Dr. Zain:** Right.

Alicia: And we try to amplify the point that clinical trials are extremely crucial in identifying effective drugs and determining optimal doses for patients. Are there any drug developments that are currently being tested in clinical trials for various stages of CTCL?

**Dr. Zain:** Thank you, Alicia, that is an excellent point. I think that experience with trying to explain a clinical trial to a patient is certainly very challenging. So, the first thing is, that I always do with my patients, is try to reassure them that this is not the end of the world and, again, clinical trials are really there to we rarely do placebo trials first of all, as you know. But they are really there for us to really provide innovative treatments to our patients and, when they start thinking about it in those terms, it becomes more acceptable to them. There are a lot of approaches right now for treating CTCL and there are a lot of clinical trials out there. I think some of the most prominent ones right now are really—as a field in oncology, we are moving toward immunotherapies. We are trying to figure out how we can harness our immune system to really fight the cancers and this is the disease model for that. Even before we had the newer immunotherapies, we had interferon, which is a very effective therapy for CTCL and it is an immunotherapy. It modifies our immune system. So now that we have a better understanding of how the immune system interacts with the cancer, we have a bunch of trials. You know, you heard of drugs out there already approved by the FDA, certainly now in trials with the CTCL, like Brentuximab, for example, but there are also other immune approaches; one of the ones that we are finding very successful at City of Hope is the Anti-CD 47 antibody, which is, again, an immune therapy, but it doesn't target the t-cells. It tends to empower the macrophages, which is also part of our immune system, to become more active against the cancer. It is sort of our innate immune system being activated. That is showing positive results and has a number of those that this trial would be open at many



centers. There are also targeted agents that are being looked at. Now that we are understanding, we have genomic understanding of tumors, or genomic mapping of tumors, we should say. We don't understand it all yet. We can actually figure out which genes have gone wrong or which pathways in the tumor cell growth have gone wrong in a particular cancer and we can try to reverse that with targeted agents. One such group of promising agents for CTCL are the PI 3-kinases and these are actually oral drugs. These are pills. So, I think the future is very promising if we can figure out a way to really—well, first, we have to figure out what has gone wrong and we are getting there. And the second thing is, how can we fix it? We may be closer to a cure, but I say that with a caveat. What most people need to understand, it's not going to be a one-shot deal. Cancer cells are very smart and they use multiple pathways to sort of outsmart our bodies so that--to allow themselves to grow uncontrollably and it will require multiple approaches to try to treat—you know, try to cure any cancer and CTCL, as well. So, a combination of all these approaches; specific to specific patients. This is where personalized medicine comes in. Maybe somebody's tumor has one pathway that is wrong combines you know versus somebody else and if we can find a cheap way to figure that out, we can certainly target therapies based on their personalized tumors. That's where personalized medicine comes in. I think that is where the future is.

**Lizette:** Right now, for treatment, since it sounds like it is more of you know the chronic disease, are people consistently on treatment, or is there in a--let's say, a remission period. Do they get off of treatment and then move back onto a treatment when it comes back?

**Dr. Zain:** So, everybody's course is different and everybody's goal of treatment is different so there are patients that are okay with a few lesions, you know and those patients we could just watch for awhile or take them off, if they have finished a course of therapy and they are left with a few lesions. You know, they may not want to start another treatment right away, For most patients, they do require constant treatment and there is a consent of maintenance in this disease, as well. We have known that from a long time, even from you know—even when we treat patients with photopheresis or when we used to treat them with—well we still do, but when—before we had newer therapies, we would always talk about maintenance. I think that has fallen—that's less talked about now, but I used to always tell patients that you will need some kind of maintenance. If photopheresis is taking care of your sensory syndrome, maybe we will reduce the frequency to once a month or once every 2 months and just kind of maintain that. And the data, again, is very unclear because this is such a heterogeneous disease, whether that actually made an impact or not, but most patients felt that it did something. We also do some you know maintenance with things like romidepsin, for example. There is—you know, we give it to them once every month, or once every 2 months, to sort of maintain their remission state, or whatever state they have achieved the minimal state of their disease; and then, if it starts to progress, then we go back on it. So, there is—you know, everybody is

different, but most patients will need some treatment and at least some follow-up with their dermatologist or their oncologist, whoever their team is, to make sure that nothing is coming back and it can be targeted as soon as it starts to show signs of you know needing clinical treatment. It also keeps them informed of any new clinical trials that may be coming by so it is important to keep in touch with somebody of this—you know, on this team, wherever you are.

**Lizette:** Sure.

**Alicia:** And you mentioned that some patients may be fine with lesions—with a few lesions. In that point, how important is it for patients to communicate effectively with their team? You know, being vocal about what they're okay with or what they would like more treatment or more understanding on. How could you encourage patients to speak openly and speak effectively with their team?

**Dr. Zain:** I think that is the most important thing. You know, confidence and the ability to discuss things with your physician and your team is the most important thing. If you don't have confidence in your team, if you feel that you can't say what you want to, I think that is not the right team for you. I always encourage that. And, certainly, patients want to seek second opinions and what not; that is fine; that should be encouraged as much as possible. I think it is very important for patients to voice their issues, or their concerns, or their thoughts to us. We do try to encourage that in our meetings with them. We also sometimes patients have some reluctance to say things to their physicians. I try—maybe—and that takes some time to get that confidence, so we always have a social worker on our team and we also have nurse practitioners on our team; and sometimes patients will tell them things that they don't want us to—they—I don't know, for whatever reason, don't want to tell us. So that is why having the team approach is so useful. It is not just a team of physicians. It is also a team of support staff and ancillary services. Social work, I think, is very important because these are chronic diseases. It does—patients do need to make time to come to their doctor's visit or their treatment visit, or whatever, and, you know, I know if I had to do that on a regular basis, I would be concerned about my job, how am I going to—my family, how am I going to take care of the things I normally need to do because this is—I'm telling my patients this is a chronic disease. You live with this so don't change your lifestyle. So, then we need to make—you know, if they need treatment, we need to make some concessions for that and that is where social work comes in very handy. So, on our team, we have a social worker; a wonderful young lady who helps our patients through these difficult challenges. Very real challenges; not just their disease.

**Lizette:** Sure; that's great. We definitely believe in the team approach and we do hear from a lot of patients that they're worried about telling you about any side effects because their medication is working and they are scared that, maybe if they tell you that they are having a bad effect towards their medication, you might take them off of it.

**Alicia:** And “you”, meaning doctors.

**Lizette:** Yeah; you meaning doctors!

**Dr. Zain:** I understand. I think we should encourage patients to tell us. We need to know what the side effects are. We need to know how our patients are suffering. You know, we do our best to guess that from our work and their symptoms, but it would be, if there is something they want to tell us, it’s very important. Our job—you know, I am not there to put patients on treatment or put patients on trial. I am there to help patients and, if there is a problem that can be fixed, maybe we change the dose, maybe we change the frequency, maybe we hold treatment for a while to help them get over that side effect. I would be—you know that’s my job to figure that out; obviously without getting their disease out of control, but if you get a chance, please encourage your audience to discuss their problems, their feelings, whatever it is that’s bothering them with their doctor. That is what we are there for.

**Lizette:** Exactly.

**Alicia:** On one of our episodes, we had a behavioral scientist, who works within the realm of healthcare, and their research was almost—it was almost staggering in regards to how many people you know either thought the doctor knew what they were experiencing, based off of this diagnosis, or felt that they couldn’t say anything because if I say anything, they will be taken off a treatment that may be working; and it is so important to have that conversation and be able to feel, comfortable with the people who are treating you. I mean, these are the people who need to know everything. I mean, these are the people who are putting together your treatment plans. I think that is one of the reasons why we kind of strive to make that a point for our listeners and for our audience because that is what helps to get the best outcome. I mean, research shows that, as well.

**Dr. Zain:** Absolutely. I mean, I always tell my patients, you and I will get to know each other very well because this is a long-term relationship. This is a chronic disease and—I mean, I have had patients who I am still in touch with. I have changed coasts. I used to be New York. I came to California. I have been back and forth a few times and I have patients who stay in touch with me. I still talk to them. They come see me sometimes, even if it is on the other side of the coast because this is a chronic disease and it is one of those situations where you do get to know the person, their families, very well. And so that is the advantage of being in this rare disease. You really get to know people as opposed to taking care of 25 patients with breast cancer every day, which is also another challenge, but not for me.

**Alicia:** Right.

**Lizette:** And there is a lot of quality of life issues surrounding cutaneous lymphoma.

**Dr. Zain:** Correct.

**Lizette:** Just you know—I guess the biggest one—itching, right?

**Dr. Zain:** Right. Quality of life is, I think, we are trying to understand that more and more. Again, lots of research needs to be done, is being done. We are trying to put quality of life questionnaires in all our research studies, but quality of life is very subjective, right? The patient has to tell us and, certainly, this is a skin disease. Cosmetics is up there. You know, you don't want to be looking rashy. You don't want to have red lesions all over your face so there is certainly a stigma attached to it no matter how educated we are. I mean, you don't want to be seen like that in the supermarket or wherever you are going. There are, sometimes, in spite of what you read, we have young patients. We have had a few young patients where looks are important and the quality of the skin. And itching, and dryness, and flaking and ulcers—all of these are really important symptoms that contribute to your quality of life. Now, we, again, this is where this multi-disciplinary approach really comes in. Itching, I think, is one of the worst symptoms you can have and, unfortunately, this is the least—we have the least amount of treatments for it that are actually effective. So, anything that we can prescribe is not going to be enough. I think what I learned from my dermatology colleagues, from my medical training, it was give things like antihistamines. We now have things like H2 blockers that can help itching, but really, it doesn't work forever. They taught me a few things. So, skin care is very important; moisturizing. So, again, as a hematologist/oncologist, I had never even remembered to mention that for my patients, but my dermatology colleagues come into the room and they talk about moisturizers for 15 minutes. Bleach baths—another way to reduce itching. Again, a scary—I was like “what” when I first heard that—a bleach bath—what are you talking about? But it makes a lot of sense because the itching, we know there is data, that itching is made worse by bacterial infections and, certainly, getting rid of that bacterial population by using bleach baths once or twice a week. It is a formula—I don't want to misspeak on it, but you can find that out from websites and, also, we have--dermatology will tell you it is a small amount of bleach in a tub of water. It is basically like a swimming pool—you know when you go to the swimming pool. And that has been effective for some patients in reducing the itching and the flaking. And then, of course, keeping your showers limited to 10 minutes and then things kinds—so there are a lot of things that we can—proper wound care; again, another important part of quality of life.

One of the things I want to mention is—this is—you know, I learned a lot about, again, from my dermatology colleagues about compounded medicines and ointments using lidocaine and silvadene, and even morphine for painful wounds, and, unfortunately, insurance does not cover that and there is—but they are effective and very helpful for patients. So, that is something that maybe we need to lobby for, for our patients...

**Lizette:** Yeah.

**Dr. Zain:** But, there are some ways to try to help these patients that are expensive for them. Out-of-pocket costs can be quite high so—but, certainly, you know, our job is to try to figure out what—how we can make our patients' lives better. That is the bottom line and quality of life is very important so we are trying to figure out how we can improve that. But there are other issues, too. There is time spent in the doctor's office. There is photopheresis is like 4 hours, you know 6 hours.

**Lizette:** Oh, wow!

**Dr. Zain:** So, treatment time is also important and, again, trying to address some of those issues--getting therapies available for them closer to home; cut down on travel time; having you know, making sure they are seen on time and not sitting in the waiting room for hours. Those kinds of things also contribute to their quality of life so they can maintain their life outside of the doctor's office.

**Lizette:** Sure. And are there other side effects from the treatments? I know that you know typical chemotherapy has side effects, but photopheresis?

**Dr. Zain:** Photopheresis is actually one of the best therapies I know because it really does not have that many side effects. There is some fatigue, but you are sitting in a chair for 4-6 hours. That could contribute to the fatigue, but most patients, you know, it doesn't increase their risk of infections; it doesn't cause nausea, vomiting. Some people will have mild nausea when they give them the photosensitizer, but it is not oral so it shouldn't matter that much. And then, the other—one other side effect from photopheresis is anemia, so they do need some—they lose some blood with each procedure. So, keeping track of that and making sure they get enough iron in supplements is all we need to do, but otherwise; it is a very safe therapy. So, the only side effect is time.

**Lizette:** Okay.

**Dr. Zain.** Yes; it is time. Other therapies—there are you know—there is fatigue with things like interferon. There is some of the other--the neurobiologics, like romidepsin and resminostat. Fatigue can be an issue; nausea can be an issue. Again, those are—we need to know if the patient is suffering so we can manage those appropriately. For romidepsin, for example, after the initial few treatments, once their disease starts to respond, I reduce the frequency of dosing so they have fewer side effects. It's things like targretin, for example, has side effects of causing high cholesterol, hyperlipidemia and thyroid issues. So, every agent has side effects and they need to be managed appropriately, but that is why you want to make sure your team is aware of what is

going on and then we can do the right blood work and whatever is needed to make sure that gets done.

**Alicia:** That's all true. Earlier, you mentioned the Cutaneous Lymphoma Foundation.

**Dr. Zain:** Yes.

**Alicia:** In addition to that Foundation and free publications that we have here at The LLS about lymphoma and the online resources we have, like chats and the community movement, which I mentioned earlier, are there other resources out there that you recommend for your patients that we may not have covered today?

**Dr. Zain:** Yes; another one is the Lymphoma Research Foundation. They also have a big CTCL. We partner with the Cutaneous Lymphoma Foundation with them. I think you mentioned the big ones, really. I tell patients not to go to the internet because that is just a random internet google search, because that is going to scare the heck out of you, I always mention LLS, LRF and CLF. Those are my pick of main go-to's because I know the information is correct. I know you guys keep it up-to-date. We contribute to that information; not me, personally, but you know experts; so, my colleagues do. So, I know that information is correct so that is the best resource for patients. For transplant, I refer them to the BMT websites, bmt.org websites, so they can learn about that from there.

**Lizette:** Doctor, what are the major concerns you hear from your patients?

**Dr. Zain:** So, patients always ask about—they come in very scared; so, the first visit is that they learned they have some kind of lymphoma. They have been told it is a rare disease. That is very common. That is the most common thing. So, the first few meetings actually are just about trying to reassure them and trying educate them about the course of this disease. I mean, I have drawn grafts. I have drawn you know—brought out survival curves—whatever it takes to kind of make them feel comfortable knowing they are not going to die tomorrow. And, believe me, that takes a while.

**Alicia:** Wow!

**Dr. Zain:** They come in with that—especially because they are coming to see an oncologist. This just scares the heck out of them. That's one major theme, I think, making them understand the course of the disease and then, the second thing, is the clinical trials issue is really—I mean, I am glad that you have this forum of trying to teach people about clinical trials. That is a huge problem. And I really, honestly, think if I had CTCL, I would go into the trials because I know the good that comes out of it. I know the bad that comes out of it, too, but I also know the good that comes out of it, but that goes with any treatment. I mean, I am not trying—so those things are kind

of important for people to understand. And then the third thing is just kind of trying to get the right physician to take care of you. It doesn't matter what the specialty is, really. And you really need a team. Those are the things I would emphasize again.

**Lizette:** I think it is good that you are highlighting the team approach because many patients feel that they only have 15 minutes with you, the physician, and they want to make the most out of those 15 minutes so, of course, we try to educate as to how to make the most of those 15 minutes, but not every patient has the other people to go to—the social worker, the nurse, somebody else that can assist them. And that is really important and I think that is really important, I think, with any of our diagnoses—that team approach because then you get, hopefully, you know a full picture of the person, the patient, and their needs, and their desires, and everything that is going on, like you mentioned.

**Dr. Zain:** Right

**Lizette:** ...the hard to get here you know. Is there a better time in the day to get here, not just the specific—you know, this is how your blood came out. This is, you know, how we are looking at your skin today and these are the treatments, but how does it all impact?

**Dr. Zain:** Absolutely; yeah; definitely. That's certainly something we have to be more considerate of and, in this time and in this day and age of kind of cost-cutting and efficiencies, I think we are going to have to come up with new ways to make sure that our patients are supported.

And, in the end, what I want to say is it's really a privilege. People ask me, "why do you do this?" I do it because I get to know people. That is really why I do it. I have met some wonderful people in my career—some really wonderful patients, and their families, and caretakers. And you see the best of humanity; you see the worst of humanity. That's what I always say. You really see the best of people if they want to come up to the plate, so to speak.

**Alicia and Lizette:** Right!

**Alicia:** And, for anybody listening as well, who we know, when you go to an oncology office like you mentioned earlier, there is a level of anxiety that goes along with you and, for anyone listening on the episode who wants to be prepared before their visit, because we always say you know write your questions down, or you know bring somebody with you just in case you forget something. And, so, anybody who is listening, they can visit [www.lls.org/whattoask](http://www.lls.org/whattoask) for printable question guides. And they are arranged by certain topics. of course, it is not a one-stop shop, but it allows you to kind of have a structure or a beginning point for what you can ask without forgetting those questions.



**Dr. Zain:** Yes; great point.

**Alicia:** Alright; well, thank you so much, Dr. Zain, for sharing your expertise with us regarding CTCL. We are sure that our listeners will learn as much as we did; and for anyone listening as well who wants more information about the resources that were discussed on this episode, be sure to check out the description of this episode below.

**Dr. Zain:** Thank you very much.