LEUKEMIA & LYMPHOMA SOCIETY®

THE BLOODLINE WITH LLS

A PODCAST FOR PATIENTS AND CAREGIVERS

Episode: 'Cutaneous T-Cell Lymphoma (CTCL): From Diagnosis to Innovation'

Description:

A Cutaneous T-cell Lymphoma (CTCL) diagnosis can raise many questions, from understanding symptoms to exploring treatment options. In this episode, we talk to Dr. Francine Foss of Yale University to break down what CTCL is, how to manage side effects, and the latest advancements in treatment—including promising immunotherapies like CAR T-cell therapy and bispecific antibodies. We also discuss the critical role of clinical trials in shaping the future of CTCL care.

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. Francine Foss, a Professor of Medicine in the Section of Hematology and Stem Cell Transplantation and Professor of Dermatology at Yale University, School of Medicine in New Haven, Connecticut. She is also the Co-Director of the Cutaneous Lymphoma Program and Co-Director of the Lymphoma Program at Yale. Dr. Foss is an internationally recognized clinician and clinical researcher with expertise in T-cell lymphomas and in stem cell allotransplantation. Welcome, Dr. Foss.

Francine Foss, MD: Thank you very much. It's a pleasure to be here to talk to you today.

Elissa: Thank you. So, our episode today is on cutaneous T-cell lymphoma, or CTCL, which is a subtype of non-Hodgkin lymphoma. Could you tell our listeners what that is and what makes it different from other non-Hodgkin lymphomas?

Dr. Foss: So, cutaneous T-cell lymphoma is a subset of the overall group of T-cell lymphomas; and it is the group of T-cell lymphomas that present clinically in the skin, i.e., patients present with skin rashes or skin tumors. This disease can also spread from the skin into the blood or into the lymph nodes in later stages. For many patients, it presents as a very minor skin rash which could be confused with eczema or psoriasis.

Now, the term cutaneous T-cell lymphoma can mean a whole number of different things because there are different types of cutaneous T-cell lymphoma. The most common type is called mycosis fungoides; and then a cousin of mycosis fungoides is the Sézary syndrome, another type. The difference between these two is mycosis fungoides is the manifestation of the disease primarily in the skin in the form of skin tumors, patches or plaques that look like eczema or psoriasis, or sometimes diffuse redness of the skin. The Sézary syndrome includes not only involvement of the skin but also involvement of the blood. So, there are actually leukemia cells in the blood; and these are the same cells that are in the skin.

Now, cutaneous T-cell lymphoma can also mean a number of other things. There might be people in the audience who have some of the rarer types such as panniculitic T-cell lymphoma, gamma-delta T-cell lymphoma of the skin. There are anaplastic large cell lymphomas of the skin. There are CD8-positive T-cell lymphomas of the skin. So, many, many different types, other than mycosis fungoides and Sézary syndrome. But for the purpose of this discussion today, let's focus only on mycosis fungoides and Sézary because these are the most common types of cutaneous lymphoma.

Mycosis fungoides and Sézary syndrome are a very small percentage of lymphomas; and there are about 25,000 to 30,000 cases in the United States, a very small number

of people have this disease. And that may explain why it is that many of you don't know anybody else who has this disease; and in fact, the research that's being done on this disease is much less than what we're doing with other types of lymphoma like B-cell lymphoma that are more common. I will say that there is a lot of research now in T-cell lymphoma and a lot of new agents that we can talk about for cutaneous T-cell lymphoma, so this does represent a very exciting time in the course of the disease.

Lizette: So, you said that really the common signs and symptoms of CTCL is skin rash or things that resemble eczema. Is that what really brings patients to the doctor?

Dr. Foss: Exactly. So, of course, there are a lot of different types of rashes and we all have rashes at some point in our lives. But CTCL can look like a whole bunch of different things; and oftentimes because it can mimic psoriasis, eczema, drug rash, and other things, people present to the doctor and for these things are most common. So, physicians may treat them like eczema, or allergic reaction, or a mild case of psoriasis. And they may get topical steroids, or they may just be observed over time.

So, many of our patients come in and say, "Well, I've had this rash for a long time. How come nobody diagnosed it till now?" And I think the answer to that question is that skin rashes are common, and only a small percentage of those skin rashes are going to be cutaneous T-cell lymphoma. So, what tips off the doctor and should also tip off the patient is when these rashes persist. So, you may use different kinds of creams, maybe topical steroids, and the rashes just aren't going away. So, persistence of the rash is one thing; and spreading to different parts of the body could be another thing that would tip us off. But like I said, many of our patients come in, and they've had these rashes for months or even years before they get diagnosed.

Lizette: And, does that mean that people usually would go to more of a dermatologist, being that it's something on the skin?

Dr. Foss: So, what usually happens is they go to their primary care doctor first, and they get that kind of first level of examination and treatment. And then if the rashes

aren't going away or the primary care doctor isn't sure about it, oftentimes they'll refer them to a dermatologist. Now, the dermatologist may try a number of different things like different kinds of creams before they do a skin biopsy. So, the only way to really diagnose this disease is with an actual skin biopsy.

Lizette: Okay. And then after they have the skin biopsy, if it is CTCL, do people have to then change from a dermatologist to see more of a hematologist/oncologist since CTCL is a blood cancer?

Dr. Foss: That's a very, very good question and there's a very long answer to the question. But, basically, just to summarize, of course, many patients present to the dermatologist. And it really depends, I think, on the dermatologist and their level of expertise and familiarity with the disease.

So, if you're in a large city such as Boston, New York, Philadelphia, San Francisco, as an example, you're in an area where there are dermatologists that are experts with this disease as well. And so, they may be very familiar, and they may see patients with the disease. But other dermatologists, they're going to need help, and they will refer them to an oncologist.

I will say that in my center at Yale, I work very closely with the dermatologists; and generally speaking, they will refer those patients into me early on in the course of their disease. And I think that's important because there are a lot of things that we're going to want to know about CTCL other than what's on the skin. We're going to know whether or not, for instance, there's involvement in the blood, whether or not there could be lymph nodes, for instance, or other things. So, I definitely think that for most patients, it's valuable to see an oncologist earlier on in the course of the disease. But I just want to give a shoutout to my dermatology colleagues who are experts in this disease, again, who are able to manage it for a very long period of time as well, until patients need to come over to oncology.

Lizette: Sure. So, what you're saying is that you really do need a biopsy to determine that it's CTCL and not some type of other skin issue.

Dr. Foss: Yes, and so basically let me just explain how we think about this disease as medical oncologists. We, of course, look at the skin biopsy and just make sure that it is mycosis fungoides or CTCL because there are other kinds of T-cell lymphoma that can also present in the skin. One example is a leukemia called prolymphocytic leukemia that's primarily a leukemic disease, but it actually can present with a similar skin rash. So, we really just need to nail down the diagnosis and make sure that it's mycosis fungoides/Sézary syndrome.

So, the rest of the workup would be that we would look at the peripheral blood by flow cytometry, which is a sophisticated way that we can look at the actual lymphocytes in the blood to see if they are atypical Sézary cells or leukemia cells. We also get scans, so we get a PET scan or CAT scans because we want to look at the lymph nodes. And depending on how extensive all of those tests are, some patients will get additional testing as well.

So, we're now in the era of molecular medicine, as you know, and we're doing all kinds of gene sequencing on tumors. And so, we certainly do actually look at molecular testing in mycosis fungoides and Sézary syndrome. We can do it in the skin, but it's very easy to actually do it in the blood now. And that's another way that we can make a clear diagnosis of mycosis fungoides/Sézary syndrome as opposed to other kinds of leukemia.

I just want to say that not all patients have blood involvement, and not all patients have lymph node involvement. So, the very, very, very early stage disease where you have only a little bit of skin involvement, maybe patches or plaques, those patients have a very low chance of having lymph nodes that are significant, or blood involvement.

So, generally speaking, initially just for staging, we like to get the test just to make sure that we've looked at everything. But if all of that is negative, as it often is for the early-stage patient, we don't need to keep repeating those testing over time. It really just depends on how the patient's doing clinically. Whereas a patient with more extensive blood involvement or who has lymph nodes on the scan, that will be something that we will follow as we treat the patient, and we will repeat all of those tests.

Elissa: Now, you mentioned the earlier stages versus maybe later stages. What is the staging like for CTCL?

Dr. Foss: The staging for CTCL is very different than for other lymphomas, and so it's something that you have to learn. It involves looking at the different compartments of the disease. So, it involves looking at the blood, the skin, the lymph nodes, and any other areas that might be involved that we pick up on CAT scan.

So, the staging is really based on the degree of skin involvement, so you have patches and plaques, tumors and diffuse redness or erythroderma. So, those are different, what we call T stages. Then you have different lymph node stages, depending on the extent of lymph node involvement; and then you have blood involvement, which, again, there's a stage for that. So B0, B1, and B2 depend on how many cells we find in the blood. And then, finally, visceral disease is defined as disease that might involve another organ in the body. And so, we put all those together – skin, lymph node, blood, and viscera – and that gives us the overall stage.

Early stage patients would have patches and plaques without significant lymph node involvement and without significant blood involvement. So, that would be like a Stage 1 or a Stage 2A. Once you have tumors on your skin, you become a Stage 2B. If you have involvement of erythroderma, so diffuse redness of your skin, then you become a Stage 3A. Depending on whether or not you have lymph nodes as well and the degree of blood involvement, you might be a Stage 3B based on those factors. If you have

involvement of other organs, then you become a Stage 4. So, all of these things kind of factor into this staging system.

Elissa: So, what is the prognosis for CTCL, and is it based on the types you mentioned earlier and the staging?

Dr. Foss: Exactly. So, the prognosis is really depending on the overall staging and the skin staging. And more recently, we've identified some other factors that are important for prognosis as well. But generally speaking, if you just have patches and plaques without extensive lymph nodes, without tumors, without blood involvement, then you have a disease that has a lifespan of a normal person, effectively. So, you don't have a disease that should cause an early death.

If you have cutaneous tumors, then your outcome is not quite as good. Of course, if you have a lot of blood involvement or you've got very extensive lymph node involvement or other organs involved, then that's a whole different story. And then, it's really more like an aggressive T-cell lymphoma where you might need more aggressive therapy. Now, that's not to say that those patients can't do well; and that's not to say that we haven't successfully been able to treat them, but it just requires a different treatment approach.

We've conducted some very large studies, international studies, registry studies where we've looked at lots and lots of patients; and we've been able to identify various biological factors, various histopathologic factors and genetic factors. Things like what we call large cell transformation in the biopsy where we see these larger looking cells can be an adverse prognostic feature. And then, also we're learning from the genetics now that we're learning that certain genes that might be mutated, like p53, for instance, might be associated with a worse outcome. And so, as we collect all of this data and all this molecular data goes into our big data banks, we're starting to sort out now whether there are different groups that we can identify, just based on the genetic mutations.

Lizette: And so, based on those genetic mutations, you're looking more at individualized medicine, so treatments that could possibly go towards certain mutations?

Dr. Foss: So, that's a very good point and it's pointing toward what we call precision medicine, where we try to identify something on the tumor cell that helps us to direct a therapy instead of giving generic chemotherapy that affects all cells the same way.

So, the answer is yes. We have identified now specific markers and, in some cases, specific genetic pathways or internal pathways within the cells that are mutated; and we've been able to develop therapies that specifically target them. The easiest to understand example of that would be a protein that's expressed on the surface of the tumor cell, say like the CD30 molecule is a good example.

We've been able to identify and create antibodies that would bind specifically to that protein, and in the case of CD30, we've been able to identify and generate toxic antibodies, antibodies that are conjugated to a toxin that can then deliver that toxin specifically to those tumor cells. And so, we have a good example of that for patients with cutaneous T-cell lymphoma, and that medication is called brentuximab vedotin. And then, we also have antibodies that don't have a toxin hooked up to them that are just naked antibodies that bind to proteins on the surface of the cell, and another example of that is a drug called mogamulizumab. Mogamulizumab targets CCR4 which is, again, a protein on the surface of the mycosis fungoides and Sézary syndrome malignant cells. And it targets the immune system to kill those cells. So, those are two very good examples of what we call targeted therapies.

Lizette: Yeah, and are these targeted therapies right now standard of care, what patients would be getting, and really what are the current treatments right now for the different types of CTCL?

Dr. Foss: So, actually, we're very lucky that we have a lot of treatments to talk about in CTCL because back, say 20 years ago, we didn't have that many. But fortunately, now we have a number of drugs thar are very active.

So, we have a drug called romidepsin that's what we call a Histone Deacetylase Inhibitor (HDACi). And that drug has been very, very active, particularly in people who have the Sézary syndrome, but also in people with mycosis fungoides. And there are a couple of patients that have been cured with that drug and have no other therapy ongoing. So, I'm very excited about that. And another drug called pralatrexate, is what we call an antimetabolite drug. That drug also has been very effective; and again, I've seen patients with extensive disease have very good responses to that. These are outpatient drugs that are easy to give, by the way. And both pralatrexate and romidepsin are given on a three week out of four schedule.

We also have the drug that I mentioned, mogamulizumab, the monoclonal antibody is a biological therapy. Again, very easy to give. The only side effect with that drug is sometimes patients can get a little bit of a skin flare or a reaction in their skin where we start the mogamulizumab. But generally, we can get through that. And again, that's a drug that has led to complete clearing of the skin and clearing of the blood in a very impressive way.

I mentioned brentuximab vedotin, the drug that targets CD30 on the tumor cells. It carries a toxin, so it directly kills the tumor cells. And again, that drug has been very, very effective for people that express that CD30 protein.

By the way, that's a test that we can get on the skin biopsy. So, if your doctor says, "Oh, I want to get a skin biopsy so I can try to figure out what the best treatment for you is, one of the things that they're going to be looking for in that skin biopsy is the expression of CD30.

Those are the main drugs that we use all the time. We also have older drugs, one of which is gemcitabine, which by itself actually is very, very active and has a very high response rate in CTCL.

And then, I'd like to talk about the newest drug that's been FDA approved, and that drug is called Lymphir™. The old name for that drug was Ontak®. So, that drug also is a targeting agent hooked up to a toxin. That drug directly targets and binds to the interleuken-2 receptor, which is, again, another protein on the surface of the malignant T cells. And It carries a toxin into the cell and kills the cell.

That drug is very new, was FDA approved several months ago and hopefully will be back in the clinic very soon. That one has a different schedule. It's given for five consecutive days every three weeks.

Lizette: Now, these therapies that you have spoken about, is the goal of therapy to be curative or is it to focus on like quality-of-life issues?

Dr. Foss: Very good question, and we would like to say that the goal of all of our therapies is try to cure the patient. I mean that's, obviously, what we're trying to accomplish. But, if we look statistically at the clinical trials with these drugs and we look at what percentage of patients were cured, it's about 10 to 15% across the board. So, there are certain patients that can be cured with these, but I would say that for many patients, it's palliation of symptoms. It's improvement in quality of life, improvement of the skin and blood manifestations of the disease. And then hopefully, if the drug works well for the patient, the patient can have a period of time off therapy before they have to start another treatment.

Lizette: Hmm, okay. And like you were saying, what are the newest treatments that are still in clinical trials?

Dr. Foss: So, yeah, there's a couple of new things. And again, the way things are moving in cancer in general are toward biologics and cellular-based therapies. It's kind of away from the conventional cytotoxic chemotherapies.

So, in CTCL, we actually have a couple of biologics that are being developed. One of them is what we call a bispecific antibody; and what that is, is that it's the targeting antibody that binds to the tumor cell. But then it's hooked up to a second antibody. That second antibody is CD3, which recruits a normal T cell and carries a normal T cell to the tumor cell. And the reason for that is that that normal T cell will hopefully recognize that tumor cell as being a foreign invader and kill it. So, it's what we call a cell-mediated therapy. So, again, that's called a bispecific antibody, and there is an ongoing clinical trial right now with one of these bispecific antibodies in CTCL that's actually shown a very high activity; and I think it's going to be very exciting to see where this clinical trial goes.

The other cell-based therapy that we have is CAR T. I'm sure that everybody has heard about CAR T and read about it as the kind of latest and greatest treatment for a lot of different types of cancer. Basically, what CAR T is, is it's taking your own normal T cells out, which we get by a procedure similar to donating blood where we take out the white blood cells and isolate the T cells. And those T cells are then injected with genes that activate them and also, a gene which targets them. So, again, those T cells are able to then go specifically to a tumor cell that has that target.

So, those cells are engineered, the way I described with the new genes. And then, they're injected back into the body. Then they can act like soldiers, and go directly to the site of the tumor, and kill the tumor. And again, this has been a very effective approach in a number of types of cancer. In CTCL, thus far we don't have an FDA-approved CAR T. But, we do have a number of clinical trials around the country that are using different types of CAR T.

Elissa: What is the target for CAR T for CTCL?

Dr. Foss: So, there are a couple of different targets that are out there. There's a CD30 and a CD5. And there was a trial that was targeting CD70, that actually showed a pretty good response rate. So, that particular CD70 CAR is now being reengineered and improved a little bit more, and hopefully that will come back into the clinic for us in CTCL very soon.

Elissa: So, what about stem cell transplant? Is that a possibility for CTCL?

Dr. Foss: Stem cell transplant actually is a therapy that we're using more and more now. So, the whole world of stem cell treatment has improved significantly over the last 5 to 10 years because, first of all, we've developed much better drugs to treat the rejection that can be associated with transplant. We've also developed ways of doing transplants from what we call haplo donors, which would be either a parent or a child or somebody who's only a half-match. So now, transplantation is open to many, many more people.

In CTCL, we've actually been very successful with allotransplant, and we've actually been able to cure about half the people that undergo a transplant. So, this is a very important modality for us right now; and we'd like to actually start seeing patients with more aggressive advanced disease earlier in the course of their disease so that we can start thinking about transplant. And when the appropriate time comes, when we get their disease under control, we can move them very quickly into a transplant.

Elissa: That is great to know. Now, you've mentioned quite a lot of treatments already, whether it's current treatments or those that are emerging or in clinical trials. What side effects can be expected from these treatments, and can they be managed?

Dr. Foss: So, the side effects of the newer drugs, the biological therapy, the cell-based therapy are a little bit different from the side effects that we saw with our older chemotherapy drugs. What these drugs can do is that they can activate the immune system to cause various things like skin rashes, for instance, inflammation in the lungs, diarrhea, those kinds of things. Those are easily managed with steroids and other

medications. Sometimes, we can get activation of the immune system and release of cytokines. In the case of CAR T cells, all of these things now are very well-managed.

With respect to some of the other drugs, the older drugs, nausea can sometimes be a problem, and lowering of the blood counts is always an issue with conventional chemotherapies. But again, we have ways of dealing with this now. We've got growth factor support; we've got prophylactic antibiotics. We've got very good nausea medicine, so I'd like to encourage patients that although we have side effects with chemotherapies and these therapies, we've gone a long way as far as being able to manage them.

Elissa: That's good to know, and it is definitely important to always talk to your treatment team if you do have any side effects coming up.

Dr. Foss: Exactly.

Lizette: Yeah. Now, are there any emerging therapies? You've mentioned a lot of different newer therapies or new modalities that you're particularly excited about.

Dr. Foss: There are a couple of new things that are being developed which are focusing, again, on specific pathways or specific enzymatic reactions within the tumor cells that are different than in normal cells that we can capitalize on. So, there are a couple of studies looking at very, very new therapies that are focusing in on different metabolic aspects of the tumor cells. And so, I think it's going to be exciting to see those.

There are a couple of those newer agents that are actually now in clinical trials for CTCL. So, take a look at clinicaltrials.gov, which gives you the information on all these clinical trials if you're interested in seeing whether there's a trial open for you anywhere near your home.

Elissa: Absolutely. And we also have our Clinical Trial Support Center for our patients that are listening. They can call in and they talk to a clinical nurse navigator and

potentially get connected with a trial that they personally would be qualified for all around the country. Thank you for mentioning clinical trials because they are so, so important.

So, our final question 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 cutaneous T-cell lymphoma?

Dr. Foss: What I would say, first of all, is that there's a lot of information online; and I would encourage patients not to pay too much attention to some of the information that talks about a bad prognosis. A lot of this information is actually old. With all the new therapies we've developed over the last five to ten years, prognosis is really changing for many patients. And again, remember when we publish this data, it's really representing 10, 15 years ago. It's not representing today.

So, the first thing I would say, don't give up hope based on things that you read online. The world is changing in T-cell lymphoma, and I talked about my excitement, about all the new things that are happening. The fact that we're using transplant more, there are more clinical trials open, and I think the other really important thing for CTCL is that a lot more physicians now are very well-educated about CTCL; and that's mainly due to the efforts on the part of organizations like LLS that really go out there and present training programs and national meetings where we present data. So, I think that there's a chance that you're going to run into very well-trained expert physicians who know this disease and also, there's a plethora of new therapies out there. So, I would say that everybody should have hope.

Elissa: That's wonderful. And what you talked about not reading things that are maybe old, that it will not apply to them makes me think of a doctor we recently spoke to that said that you are not a statistic. And these things may not apply to you. Everybody is different, and you've talked about so many different treatments out there and then, so many different types and how it could affect you. So, we really

appreciate you coming on with us today, and I think really giving hope to patients that are affected by this disease and so they can go back to their doctors and talk about these different treatments and see what would work best for them or get onto a clinical trial.

And so, again, thank you so much for being here with us today. We really appreciate you.

Dr. Foss: Thank you so much for the opportunity, and good luck to all the patients.

Elissa: Thank you.

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.

Did you know that you can get more involved with *The Bloodline* podcast? Be sure to check out our Subscriber Lounge where you can gain access to exclusive content, discuss episodes with other listeners, make suggestions for future topics, or share your story to potentially be featured as a future guest. You will also receive an email notification for each new episode. Join for free today at TheBloodline.org/SubscriberLounge.

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

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

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

Have you or a loved one been affected by a blood cancer? LLS has many resources available to you – financial support, peer-to-peer connection, nutritional support, and more. We encourage patients and caregivers to contact our Information Specialists at 1-800-955-4572 or go to LLS.org/PatientSupport. You can find more information on cutaneous T-cell lymphoma at LLS.org/Lymphoma. These links and more will be found in the show notes or at TheBloodline.org.

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