LEUKEMIA & LYMPHOMA SOCIETY®

THE BLOODLINE WITH LLS

A PODCAST FOR PATIENTS AND CAREGIVERS

Episode: 'Innovative Therapies: Transforming Non-Hodgkin Lymphoma Care'

Description:

The treatment landscape for non-Hodgkin lymphoma has significantly evolved over the past few decades. With groundbreaking advancements in CAR T-cell therapy and bispecific antibodies, researchers are making strides toward curative treatments and enhancing patients' quality of life.

In this episode, we speak with Dr. David Bond from The Ohio State University about the latest developments in treating both aggressive and slow-growing non-Hodgkin lymphomas. He discusses innovative, newly approved therapies for patients, as well as how improvements in supportive care better manage the physical and emotional side effects of treatment.

Transcript:

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

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

Elissa: Today, we will be speaking with Dr. David Bond, a Clinical Associate Professor of Internal Medicine in the Division of Hematology at The Ohio State University in Columbus, Ohio. Dr. Bond's clinical focus is in the treatment of Hodgkin and non-Hodgkin lymphoma; and he is involved in clinical and translational research, investigating prognostic factors and novel therapies in lymphoma. Welcome, Dr. Bond.

David Bond, MD: Yeah, thank you, Elissa and Holly. I'm very happy to be here.

Elissa: So, our episode today is on non-Hodgkin lymphoma. Could you please tell our listeners what that is and what distinguishes it from Hodgkin lymphoma?

Dr. Bond: Yes. So, this is usually one of the first questions that people ask when they're coming to see me, and they have any kind of non-Hodgkin lymphoma diagnosed. And Hodgkin lymphoma has this particular name, more for historical reasons. It was the first type of lymphoma that was recognized, and so it was named after one of the physicians that first described it. And then, we subsequently learned that there's many kinds of lymphoma, in fact over 40 kinds of lymphoma. And then, all of the other types that were subsequently discovered really fell under this term of non-Hodgkin lymphoma, which really isn't very descriptive, but kind of the terminology that's been in place.

And so, I usually like to take a step back and just say, what is lymphoma as a broad term? And essentially, it refers to any kind of blood cancer that comes from a type of immune cell called a lymphocyte. We have different types of lymphocytes in the body, and two main kinds, B and T lymphocytes; and I think that, knowing the normal precursors helps us to understand these different types of lymphoma that can be diagnosed in mostly non-Hodgkin lymphoma with about 10% of the cases falling under this category of Hodgkin lymphoma.

Holly: Dr. Bond, we know that lymphomas are either categorized as slow growing or aggressive. What are the differences between the two?

Dr. Bond: Yeah, typically with lymphomas and non-Hodgkin lymphomas, we have these two broad categories; and so, there's a category known as slow growing. You'll also hear the term indolent for that category. And then the other broad category is aggressive, and the distinction is based on the typical pattern that we see with them with these aggressive lymphomas being ones that tend to grow fairly quickly or more quickly compared to the less aggressive or slow-growing lymphomas. And the less aggressive lymphomas tend to grow more slowly, and many times they're diagnosed just more of an incidental diagnosis even because of just the slow nature that they have. So, that's one of the broad kind of distinctions, but there's multiple types of non-Hodgkin lymphoma in both those categories. And I will say that even within each

individual subtype, it can behave differently. So, in some cases, a lymphoma, even though it's classified as slow growing, can be fairly fast growing. In other cases, they can be a lot more indolent-behaving. So, it really does vary a lot from person to person.

Elissa: So, what do you mean by indolent, just for listeners who may not know?

Dr. Bond: Yeah, so, with indolent or slow-growing diseases, these are diseases that in many cases can be present. Some cases find it because somebody has a test done or a CT scan done for other reasons; and they notice an enlarged lymph node, and they have a biopsy that diagnose this type of disease.

In some cases, people can go for many years and really not see a significant change in the size of the lymph node; and it really can be something that is there in the background but not causing necessarily any issues or symptoms.

Elissa: Okay. And could you talk about the common subtypes with both the slow-growing and the aggressive lymphomas?

Dr. Bond: Yeah, starting with the slow-growing lymphomas, the most common subtype is known as follicular lymphoma. This is a disease that comes from our normal B cells. And one of the things that I mentioned that we have the two types of lymphocytes mainly in the body, B and T cells. And for various reasons, 95% of lymphomas come from the B cells; and so really most of the diseases that we're going to be talking about that are more common are from these B cells.

So, follicular lymphoma is the most common. It comes from B cells. Other fairly common types of the slower-growing or indolent lymphoma include one called marginal zone lymphoma, which again comes from the B cells. And then another disease called lymphoplasmacytic lymphoma can be associated with a protein that's being produced by the lymphoma cells. And in that case, it's known as Waldenström macroglobulinemia.

Elissa: And the aggressive subtypes?

Dr. Bond: So, the most common aggressive subtype of non-Hodgkin lymphoma is known as diffuse large B-cell lymphoma; and that's actually the most common overall subtype of non-Hodgkin lymphoma that we see. So, more common than any of the individual other types.

There are a number of diseases that are really closely related to this diffuse large B-cell lymphoma but have a specific category or term for them. The somewhat more common type of aggressive non-Hodgkin lymphoma is called Burkitt lymphoma which looks differently under the microscope and is a really distinct disease. So, Burkitt lymphoma, diffuse large B-cell, I'd say, are the two main categories of aggressive lymphoma; but then there's a lot of other situations where we have specific terms for a type of aggressive lymphoma that's very similar to diffuse large B-cell lymphoma but that may have its own name.

For instance, there's a disease called primary mediastinal B-cell lymphoma which is more common in younger patients generally; but it can present with an enlarged lymph node in the chest or mediastinum. And it looks under the microscope similar to the diffuse large B-cell lymphoma, but it has its own term because we've recognized that it has a distinctive presentation and age range and biology.

Elissa: Okay. Now, what is the goal of treatment for slow-growing and aggressive lymphomas? Are any curable, or is the goal more on quality of life?

Dr. Bond: So, for the aggressive lymphomas, the goal of treatment, in general, is curative; and these are diseases that, if they're not treated, they will grow very quickly and generally are fatal if they're not treated over months or years. But for really all of these, the goal with giving treatment is to cure the lymphoma, so to get it into remission and in many cases it will not recur if it is in remission.

With the slower-growing lymphomas, it's a bit different for multiple reasons. One of the reasons is that, in some cases, like I mentioned, these can be diseases that don't change and don't cause symptoms for fairly long periods of time. So, for some individuals, they can go for many years and not ever require any treatment. In many cases, people can have a life expectancy that's the same as somebody that doesn't have that disease, even without requiring treatment. So, in that case, there's not always even a need for treatment.

And we do have many treatments that are effective for these diseases, but these are diseases that can come back, even after longer periods of time. We think that's related just to the fact that they are slower growing and so, they may somehow be able to be dormant in the body for longer periods of time and then come back.

So, we don't generally call the treatments curative for these because there is always a possibility, even after longer periods of time, that they could come back. But that being said, in many cases with treatment, patients have very good or excellent outcomes. And not only does the treatments help quality of life, but they can put the lymphomas into remission for very long periods of time or, perhaps, in some cases even, put the lymphoma into remission for one's entire lifetime and never come back.

Holly: So, let's discuss some current treatments. What are common treatments for non-Hodgkin lymphomas, and are there different treatments for aggressive versus slow growing?

Dr. Bond: Yes, so that's a great question. And as you can imagine with so many kinds of non-Hodgkin lymphoma, the treatments do vary widely; and there is overlap between how we treat different types of non-Hodgkin lymphoma, but there also are differences, particularly as you highlighted, differences between how we treat the more aggressive and the slower-growing lymphomas.

One of the treatments that we use for most types of lymphoma, that's become really a game-changer over 20 years now, is a drug called rituximab, which is one of the first

immunotherapies that's developed for cancer. But it's a monoclonal antibody, and it targets this protein on B cells, including lymphoma cells that are derived from B cells. And it can be given by itself and for some of the slower-growing lymphomas, that's a common treatment to give the rituximab by itself; but it also can be combined with chemotherapy drugs. And so, for the more aggressive lymphomas, generally, we would be giving that in combination with more conventional chemotherapy-type treatments or drugs.

Holly: And are there more avenues, such as CAR T-cell therapy or bispecifics, available for any non-Hodgkin lymphomas?

Dr. Bond: Yeah, you mentioned a couple of the newer treatments that I wanted to talk about today. And one of the things, to take a small step back, is just again that the vast majority of these come from B cells. And the rituximab, as well as a lot of the other newer immunotherapies that now have been approved in the past five years or so, these really target specifically B cells. So, for the less common T-cell lymphomas, none of these are part of the treatment because they're really targeting something that's on these B cells, which isn't present on these type of T-cell lymphomas.

For the B cell lymphomas, particularly maybe focusing more on the aggressive lymphomas, with chemoimmunotherapy, so with rituximab and chemotherapy drugs, there's a very high rate of cure initially with those treatments. It's still not 100%. In some cases, these either can come back or not go into remission with the initial treatment.

And in those instances, that's where we have these newer types of therapy that are now approved and available that can be used that, in many cases, can have a much higher rate of going to remission than previous treatments and, particularly in the case of this CAR T treatment, can even be a curative treatment for these diseases that haven't been cured with the initial chemoimmunotherapy.

Holly: That's great.

Elissa: So, are there approved treatments then in either CAR Ts or bispecifics for non-Hodgkin lymphomas or are they still in trials?

Dr. Bond: Yeah, the most common type of non-Hodgkin lymphoma, diffuse large B-cell lymphoma, there are three different CAR T treatments that have been approved; and the CAR T treatment is a type of therapy, which is a really amazing technology. It essentially involves taking a person's T cells, a type of their immune cells, and engineering them or modifying them to be able to attack or to target a protein that's on the tumor cell. And then, to give them back to a patient and have their own cells that have been modified be able to then go and attack the tumor.

The first studies were actually in a disease called CLL, or chronic lymphocytic leukemia; but really where it saw the biggest breakthrough success was in acute lymphoblastic leukemia (ALL), which is a type of leukemia that's more common in children, and so the first use was really in pediatrics.

But really, the second main use and what led to approval of three different drugs was in diffuse large B-cell lymphoma. The generic names for them are a little bit of a mouthful, but one of the drugs is called axicabtagene ciloleucel. The trade name is YESCARTA®. There's another drug called lisocabtagene maraleucel, which is called Breyanzi®. And then there's a third drug called tisagenlecleucel, also known as Kymriah®. So, all three of these CAR T drugs are approved for diffuse large B-cell lymphoma, and they also are, in some cases, approved for other closely related types of aggressive lymphoma like, for instance, primary mediastinal B-cell lymphoma.

And in the case of two of them, they're approved as a second treatment. So, if somebody has treatment with chemoimmunotherapy and then requires further treatment because the lymphoma either wasn't in remission or came back, the YESCARTA and the Breyanzi are currently approved as the next treatment to be offered.

Elissa: I think that's often a question of our patients is can they get it as first-line treatment, and it doesn't seem to be available as first-line treatment for any of these indications.

Dr. Bond: Yeah, not currently. There are studies looking at using it as a part of initial treatment in certain situations, so that's something that's definitely being studied. But at least right now currently, we're still using chemoimmunotherapy as the initial treatment. But that could very well change in the next coming years.

Elissa: Okay, and what about bispecifics?

Dr. Bond: Yeah, so the bispecific antibodies are a type of technology similar in some ways to the monoclonal antibodies like rituximab. But instead of just targeting a protein that's on a tumor cell, they also have a component which targets a normal part of our immune system and brings that in proximity to the tumor to cause it to activate these immune cells and work as more of active immune therapy that brings our T cells to attack the cancer cell.

There are currently three of these types of therapies approved that target the protein CD20, which is the same protein that the drug rituximab targets, as well as targeting CD3, which is on our T cells, so in that part of our immune system. And so, these drugs help to bring our immune cells to attack tumor cells that express this B cell protein, CD20.

And they're being used in multiple types of non-Hodgkin lymphoma currently. And currently the approvals for them are in diffuse large B-cell lymphoma and in follicular lymphoma, so, the most common type of aggressive and then the most common type of indolent lymphomas of all.

Elissa: Okay, great.

So, we discussed earlier the goal of treatment for some lymphomas is more on quality of life. And we all know that side effects from treatment or the cancer itself can really

impact quality of life for patients. What side effects are non-Hodgkin lymphoma patients usually having, and what can be done to manage them?

Dr. Bond: It varies so much just because there's so many types of non-Hodgkin lymphoma and even within a certain type, the way that it manifests or the areas that are affected can vary so much from person to person. Everyone's different; and the different diseases can vary quite a bit as far as just what symptoms people are experiencing before they start treatment and the types of treatment, how intense they are and how much they are expected to cause side effects.

I think the range can be fairly broad. And so, going from the follicular lymphoma or other slow-growing lymphomas, in some cases the rituximab can be used by itself as an immunotherapy. And it's an IV medication. It may cause some fatigue, but generally is very, very well tolerated and very little in the way of side effects.

Going more to the other extreme, for instance, with one of the aggressive lymphomas, Burkitt lymphoma, where we use multiple chemotherapy drugs along with rituximab, and it's really a fairly intense conventional chemo-type treatment where it causes more of the typical chemo-type side effects that you would think of like hair loss, fatigue, tiredness. So, a very wide range and each treatment can vary a lot.

I think one of the good things, not only that we have treatments, but like the immunotherapies that tend to be a lot milder than the conventional chemo drugs, but even when we do use conventional chemo drugs, we have a lot more at our disposal to prevent nausea, to help bring up the white blood cells, to limit the amount of times that those are low, to really help support people through treatment. So, I think the supportive care has really come a long way over the past 20 years or so and so, these are a lot better tolerated than they would have been 30, 40 years ago. And so I think because of that, these are generally very manageable treatments, even across the whole range of intensities.

Elissa: That's good to know. And I know we talk a lot on the podcast and on other programs how important it is to communicate with the treatment team, to let you know that they are having these side effects so that you can hopefully be able to help them manage it.

Dr. Bond: Yeah, absolutely. I think there's a lot that we do just on a preventative basis. But we can also make adjustments, and there's a lot that we have at our disposal to help with symptoms and side effects that people are having. So, definitely really important that we know what's going on as we're prescribing the treatment.

I had somebody recently that was concerned because they had more side effects early on; and then there were adjustments, and they weren't having so many side effects. And they said, "Well, if I'm not feeling bad, maybe this isn't working." But, it really doesn't work that way. And I think that that's kind of a perception. Some people think that, because they're getting chemotherapy treatments, that they should have a lot of side effects or symptoms. But really our goal is to try to minimize that and make the quality of life as good as possible going through the treatment. And there's a lot we can do if we know what's going on and what people are experiencing.

Elissa: Yeah, I think that's definitely been a perception of cancer patients going into treatment that it's going to be absolutely miserable all the time for months or years. And so, it is always good to know that these symptoms can be managed, at least on some level, to make their quality of life certainly better.

Dr. Bond: Yeah, absolutely. And I think sometimes people are surprised once they get started on treatment because they're expecting it to be so much worse than it actually is. I think sometimes that perception can really make it more daunting at the outset when somebody's looking at starting treatment.

Holly: So, let's talk a little more about living with non-Hodgkin lymphoma, whether it's slow growing or aggressive. It can have emotional, as well as physical impacts for

patients and their caregivers. So, how are you working with patients to address these impacts to their lives after a diagnosis?

Dr. Bond: Yeah, that's a great question and I think that's definitely with any cancer diagnosis, that's a big factor, but particularly with lymphomas. And these happen across such a wide age range and it's different, depending on each step of life that we're in. But in many cases, people that are coming in are young and just starting their lives, on their own; and then they're facing this cancer diagnosis and how to cope with all of the changes that are happening, is a really important part. And I think, it's not just physical going through treatment. It's definitely the impact on our lives, our emotions, and our relationships is a huge part of the experience of going through treatment.

One of the reasons that I went into this field, when I was in my early 20s, I was diagnosed with a non-Hodgkin lymphoma; so, I can relate to it from both standpoints. But I know for me personally, the journey that I went through, and I think one of the things for me is just to acknowledge from the outset that that's an important part and that it's a normal experience for it to not be an easy adjustment to kind of having your whole world upended with this diagnosis.

But, like you said, there are things that we can offer. We can help with the physical symptoms, which go hand in hand with the emotional component. And I think a lot of our centers also have resources, have people that are available to help navigating certain situations or providing specific resources and then also helping to connect with other people that have gone through similar experiences.

And for me, the LLS was a great resource because they have a program that connects you with families or patients that have had a similar diagnosis and gone through it (*Patti Robinson Kaufmann First Connection® Program)*. And so, I think that can be really helpful, and I've had other patients that really have appreciated having that resource available.

Holly: Yeah, it's definitely important to look at this holistically and not forget that even though you are going through these physical challenges, trials and tribulations, that the emotional part is just as important.

Elissa: Yeah, and it's nice to see, actually, as unfortunate it was that you went through non-Hodgkin lymphoma to see an oncologist that went through the same disease that they're, treating patients for. And so, I think that's an interesting way to be able to relate to your patients and also certainly relate to the emotional impact of cancer because you've already been through it.

Dr. Bond: Yeah, yeah. I'm definitely not the only oncologist in the field that's had that diagnosis.

Elissa: Right.

Dr. Bond: And I think that's one of the things that you realize is, for patients I think to know is that there's a lot of people that have gone through it and you may never have known it until you start to talk to people. So, I think there's really a lot of people out there that can in some ways at least relate, and all of our lives and experiences are unique to us. But there's a lot of people that have gone through similar situations before. And in many cases, you may not know it, and so, I think sometimes it helps to hear from the perspective of somebody that's gone through something similar before.

Elissa: Yeah, absolutely. I remember when I was in treatment for acute myeloid leukemia, I found out months into treatment that one of the nurses in the infusion room also had had a blood cancer; and I think it was almost an immediate connection. I was like, "Wow. You not only work here, but you really understand on a different level what I'm going through." And I've never forgotten it, even years later.

So, we have now discussed current treatments as well as managing side effects. Let's talk about emerging therapies for non-Hodgkin lymphoma. Are there any new treatments or those on the horizon that you're particularly excited about?

Dr. Bond: Yeah. The two big categories that already were highlighted, that are approved for some types of non-Hodgkin lymphoma, I think these are two treatments that are really exciting – the CAR T therapy and the bispecific antibody therapy. And these are kind of broad terms. We've explained, I think, some of how the current treatments and products that we have are made up. But then there's work looking at newer technologies, newer constructs of similar types of ideas but different applications.

And so, there's work looking at these in other types of non-Hodgkin lymphoma where they're not currently approved. They're looking, in the case of the bispecific antibodies, using them as more of a combination with other treatments. Including even as a first treatment. There's studies looking at whether that improves adding the bispecific antibody to chemotherapy initially for diffuse large B-cell lymphoma, for instance, but other types of non-Hodgkin lymphoma are being looked at as well.

Really, there's a lot that is on the horizon with studies looking at new ways to use those two therapies. And so, I think those are the two categories that have already been shown to be effective; but I think there's potentially a lot more role for these to be incorporated into treatment.

Elissa: Yeah, that will be really exciting as we move forward and see where they can go.

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 non-Hodgkin lymphoma?

Dr. Bond: The first thing is that, really, you're not alone going through this**.** All of us have a lot of people there that are there to support us and you really can find that out after a cancer diagnosis. But certainly, the clinic team, the physicians, nurses, nurse practitioners are there to help get you through the treatment. I think the amount of breakthroughs that have come in this specific disease is really amazing over the past

20 years. I think there's a lot more that we have to offer today than we would have been able to offer in the past. And then also, even, like I mentioned with supportive care with medications to help minimize symptoms and side effects, that's come a long way as well. So, I think the experience going through the treatment has gotten better as a result of that in many cases as well too.

Elissa: Absolutely. Well, thank you so much, Dr. Bond, for joining us today and talking all about non-Hodgkin lymphoma. I'm sure you've given so much hope to patients listening and their loved ones to hear all about the current and emerging treatments and all the possibilities out there. And also, just managing side effects, to be able to give them that good quality of life as they go through treatment. And so, again, we really appreciate you being here with us.

Dr. Bond: I'm very grateful for the invitation and happy to be back anytime.

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.

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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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