LEUKEMIA & LYMPHOMA SOCIETY®

THE BLOODLINE WITH LLS

A PODCAST FOR PATIENTS AND CAREGIVERS

Episode: 'Accelerating Hope for Aggressive Non-Hodgkin-Lymphoma'

Description:

Delve into the complex landscape of non-Hodgkin lymphoma research, where a cure is pursued amidst a backdrop of over 100 subtypes of this disease.

In this episode, Dr. Kieron Dunleavy, of MedStar Georgetown University Hospital, breaks down the differences in treatments, prognosis and goals for both slow-growing and aggressive subtypes of non-Hodgkin lymphoma. Discover the remarkable momentum of scientific progress that increased the understanding and management of lymphoma, igniting a renewed sense of hope for patients and their loved ones.

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 to Dr. Kieron Dunleavy, a Professor of Medicine at Georgetown University and the Director of the Hematologic Malignancies Program at the Lombardi Comprehensive Cancer Center, MedStar, Georgetown University Hospital in Washington, DC.

Dr. Dunleavy is a medical oncologist who specializes in the treatment of aggressive and slow-growing lymphomas, including those in the adolescent and young adult population as well as chronic lymphocytic leukemia or CLL. As the principal investigator for several clinical trials, his work combines active clinical research and patient care with the goal of developing new treatments that will improve outcomes for people with lymphoma. Welcome, Dr. Dunleavy.

Kieron Dunleavy, MD: Hi, and thank you very much for inviting me here today.

Elissa: So, our episode today is on non-Hodgkin lymphoma, particularly the aggressive subtypes. Could you explain to our listeners what non-Hodgkin lymphoma is?

Dr. Dunleavy: Yeah, sure. Non-Hodgkin lymphoma is a type of cancer or malignancy of the lymphatic system. We have lymphatic tissue all over our bodies. And lymphomas typically come from lymphocytes. We have B lymphocytes and T lymphocytes, and these are the origins of B cell lymphomas and T cell lymphomas.

It's a very complicated area. There are a lot of different types of lymphomas. About 85% of non-Hodgkin lymphomas are B cell lymphomas, and about 15% are T cell lymphomas. And interestingly, in different regions of the world, the proportion of B cell and T cell lymphomas can be different. So, in Asia, for example, there is a higher proportion of T cell lymphomas than in the US and Europe. So, there are geographical differences in the incidence of these diseases.

Elissa: Well, that's interesting. Why is that?

Dr. Dunleavy: So, some of it is understood. Some of it is not. Some lymphomas are associated with viruses which are more prevalent in certain geographical areas, and that explains some of it. But we're not entirely clear why this difference occurs, and it's under investigation with epidemiologists and with different cancer researchers to try to understand why there's a different proportion of non-Hodgkin lymphomas, depending on which part of the world you live in.

Lizette: And since we're focusing on the aggressive subtypes for this discussion, could you share how they differ from the slow-growing subtypes of non-Hodgkin lymphoma? I know that there's so many subtypes at this point.

Dr. Dunleavy: Yeah, so it's really over 100 subtypes of non-Hodgkin lymphoma.

Elissa: Wow.

Dr. Dunleavy: We have two classification systems. We've got a World Health Organization (WHO) classification of lymphomas, essentially. And there's another classification system called the International Consensus Classification System (ICC). So, in both of those systems, they list all of the different types of non-Hodgkin lymphomas, so we can broadly divide non-Hodgkin lymphomas into aggressive and indolent (slow-growing); and it's, of course, a lot more complicated than that.

But in short, the aggressive lymphomas, they present over a short period of time, meaning that people are unwell for sometimes days, sometimes weeks, not typically months. So, the onset of these lymphomas is very rapid, and they need urgent treatment; so treatment needs to be initiated very, very quickly.

But, the good news about aggressive lymphomas is that they are very curable diseases; and the majority certainly of diffuse large B cell lymphoma, which is the most common type of aggressive B cell lymphoma, the majority of these can be cured with current treatments that we have. There are some rare types of aggressive lymphomas such as Burkitt lymphoma, which, again, is highly curable and other aggressive lymphomas, as well, which are not as common.

In contrast, indolent lymphomas can present over a very long period of time. So, when I see a new patient with indolent lymphoma, it's very common for them to say that they have had lymph nodes for a number of months or sometimes years or they've had symptoms that have been ongoing for a long duration of time. So, the two types of lymphomas behave very differently.

In contrast to aggressive lymphomas, we don't think of lymphomas that are indolent, for the most part, as being curable. They're highly treatable, but our expectation is that these, most of the time, become like chronic diseases where there are excellent treatments for them. They can reduce the amount of lymphoma, but there's a high chance that the lymphoma will come back in some shape or form.

I would say that with all of the new treatments that are being developed, some of these ideas about indolent lymphoma as being incurable are shifting and changing a little bit. And the most common type of indolent lymphoma is follicular lymphoma; but when we look at recent studies, there is a proportion of people who receive current treatments that we use for follicular lymphoma who end up having very long complete remissions, and we have to wait for longer to follow these patients out for decades. But, there certainly may be a proportion of these who are cured and their disease never comes back.

Elissa: Now, for those slow-growing, or indolent, subtypes that you were talking about, can they ever transform into a more aggressive lymphoma?

Dr. Dunleavy: Yes, so they can. Again, the most common type of indolent lymphoma is follicular lymphoma. There's another similar disease called chronic lymphocytic leukemia (CLL). It's called a leukemia, but it has a lot in common with indolent lymphomas; and both follicular lymphoma and chronic lymphocytic leukemia, can transform into a more aggressive lymphoma. Follicular lymphoma can transform into diffuse large B cell lymphoma. That's not very common. If we look at all patients with follicular lymphoma, the rate of transformation is somewhere between 1 to 2% per year.

It's an area that's under investigation. We don't fully understand why some people are at higher risk of transforming to a more aggressive lymphoma. The same is true of CLL. CLL can transform into an aggressive lymphoma; and when it does that, it's called Richter's transformation. Again, that is pretty uncommon; but it can happen. And, of course, when that happens, we have to focus on treating the aggressive component of the lymphoma because that is the one that is moving more rapidly and needs urgent therapy initiation.

Elissa: Are you able to do anything to prevent that transformation into a more aggressive lymphoma?

Dr. Dunleavy: That's an excellent question; and the answer is we don't know.

Elissa: Yeah.

Dr. Dunleavy: But there are a lot of groups around the world that are studying this because, of course, if we could prevent people from transforming, that would be extremely important in therapeutics. But at this point in time, we don't have an answer in terms of how we prevent that.

I think we need to really understand why this happens; and so much work is being done both in clinical trials, but also in the lab as well. Scientists are looking at these questions and studying transformation and seeing how these transformed cases are different in terms of their genetic makeup compared to cases that don't transform. All of these things are being done, so hopefully we'll be able to answer that question as we do more research, and we understand what's going on better.

Lizette: Sure. You mentioned B cell and T cell, and I know there's also NK cell, natural killer cell. Are T cell and natural killer cell lymphomas considered more aggressive?

Dr. Dunleavy: Yeah, so in general, T cell and NK cell lymphomas are very rare. But, they are highly aggressive lymphomas; and, unfortunately, the outcome in general for T cell lymphomas is not as good as it is for B cell lymphomas.

T cell lymphomas are rare, and that's one of the challenges in making progress and understanding them better and also developing new treatments for them. T cell lymphomas are more common, as I said, in some parts of the world than they are in the US. But I think in the US, it's very important that people who are studying T cell lymphomas, especially in clinical trials, that they collaborate and work very closely together. And there are T cell lymphoma consortiums because when you have a rare lymphoma, you need all of the people who are focused on T cell lymphoma research to work together because these cases are not common. So, it's best if people pool all

their resources and thoughts and clinical trials together and move together in one direction, especially in T cell lymphomas.

Lizette: Right, and there are clinical trials for these more rare types of lymphomas, right?

Dr. Dunleavy: Yeah, there are. They tend to be at bigger centers. There are a few centers around the US that really specialize in T cell lymphomas. I think it's easier to access clinical trials in B cell lymphomas in smaller centers. But for the T cell lymphomas, because they're rare, there are few super specialized centers that really excel in T cell lymphoma research.

Elissa: Now, what are the common signs and symptoms of the aggressive subtypes of non-Hodgkin lymphomas, and how is it usually diagnosed?

Dr. Dunleavy: Yes, so, you know, one thing about lymphomas is that you can have a lymphoma in any part of your body. The way that they present is a huge spectrum of symptoms and signs. I would say that most people will notice that they have enlargement of a lymph node or several lymph nodes. We have lymph nodes all over our body, but the areas where we can appreciate them if they get enlarged are typically in the neck area, in the axillary area underneath the arms, and also in the inguinal (groin) areas.

So, when people present with aggressive lymphoma, they will often say, "I noticed a swelling in my neck two or three weeks ago. I went to my primary physician, and we thought it might be an infection; and I got antibiotics, and the swelling didn't improve. It actually got worse." And they're referred to a specialist, and they get imaging and a biopsy and the biopsy comes back showing aggressive lymphoma.

But as I said, because they can originate in any part of the body, they can present in lots of different ways. So, most of the time they come from B lymphocytes, and you see lymph node enlargement; but they can involve organs in our body. For example,

we see a lot of patients here who are younger and between the ages of 15 and 35. When they present with lymphoma, a high proportion of them will have a type of non-Hodgkin lymphoma called primary mediastinal B cell lymphoma. Those patients are usually female, and they almost always have a large mass in their chest. Their symptoms are typically, "I've noticed some shortness of breath, some chest pain," and sometimes they'll have other symptoms as well. You can have lymphomas in the brain, and people who have lymphoma in the brain will present with very different symptoms to other lymphomas that are outside the brain, obviously.

To answer your question, most of the time people will have lymph node enlargement; but there are lots and lots of other types of presentations as well.

Then, in terms of the diagnosis, a diagnosis of lymphoma is done by a lymph node biopsy. And when we work with our pathologists, they always impress on us that it's really important to have adequate tissue to make a definitive diagnosis. So, the entire lymph node, if they have lymph node enlargement, needs to be evaluated by a pathologist.

When you work closely with pathologists, you appreciate that if they just get one tiny piece of the abnormal tissue with a needle biopsy, they're very limited in how they can interpret it. I mean, they can tell us what they see and what they find, but they really like to have more tissue. And in my experience, it's really important to do that because when we do the needle biopsy and then we do an excisional biopsy, we get so much more information with the excisional biopsy. It might not change the next steps, but sometimes it does. So, it's really important to do that whenever we can.

I can't emphasize how important it is to have a proper diagnosis when you have lymphoma because there are over a hundred different subtypes. Even within those subtypes, there are different forms of different subtypes. So, it's really critical that the pathologist is an expert in looking at lymphoma cases and is able to distinguish all of

these different subtypes because it can really make a difference to the treatment that we select.

For example, it's easy, most of the time, for the pathologist to say it's indolent lymphoma or it's aggressive lymphoma, it's follicular, or it's diffuse large B cell lymphoma. But there are a lot of cases that are in between and in some kind of a gray zone. At our institution, we have a weekly meeting with our pathologist where we review all of the new cases. And every week we come across a few of these cases where we really have to discuss them in detail with the pathologist because they don't easily fit into one of these diagnostic categories. And that is very informative on how we should approach treatment sometimes.

Elissa: You mentioned earlier that those enlarged lymph nodes can be anywhere in the body. And if there are multiple places in the body, that can be then classified as Stage IV. Stage IV cancer can sound really scary, but it doesn't mean what Stage IV cancer means for a solid tumor, correct?

Dr. Dunleavy: Yeah, that's exactly right. For solid tumors, staging is hugely important because those diseases in early stage can be removed surgically; and sometimes what's called adjuvant therapy is required. But, when those diseases become Stage IV, they are typically associated with a very poor prognosis.

It's really different with lymphomas. The stage is important in diffuse large B cell lymphoma, the most common non-Hodgkin lymphoma. It does predict to some degree how people do. There's an index called the International Prognostic Index or the IPI Score. It looks at five different factors. One of them is advanced stage, but it's really not as important as it is in some of these solid tumors. And what's really much more important is the cell type. So, for example, diffuse large B cell lymphoma is a highly curable lymphoma, even if it is Stage III or Stage IV, whereas some other lymphomas have a low cure rate because of their cell type.

So, while stage matters somewhat, it's not as important. But a lot of people, when they get a diagnosis of lymphoma, they're very fixated with their stage. So, when we see a patient for the first time, we often spend quite a bit of time just explaining that, yes, it is important; but it's much more important that you've got a cell type that is very sensitive to treatment and is likely going to go away with the treatment, irrespective of the stage.

Lizette: Doctor, you mentioned earlier, when you were talking about the slow-growing, or indolent, types versus the aggressive types that aggressive forms of lymphoma are potentially curable whereas the chronic, indolent forms, you manage. So, basically the goal of treatment between the aggressive and the slow growing are different, right?

Dr. Dunleavy: Yeah, they are different. For the most part, with aggressive lymphomas, the goal is cure; and typically, the treatment duration is short in terms of it being 18 weeks of treatment. Whereas in indolent lymphomas, when people do need treatment, and I would say that a very high proportion of people with indolent lymphoma don't need treatment, it's best to pursue what's called a watch and wait approach where treatment is not instituted, or it's deferred until a time where the disease is starting to move very rapidly.

But when patients with indolent lymphoma need treatment, the treatments are often chronic. One really good example of that is chronic lymphocytic leukemia, or CLL, where a very high proportion of people, when they do need treatment, they receive a class of drug called BTK or Bruton's tyrosine kinase inhibitors, and those are usually continued until the disease comes back.

That's a distinct difference in terms of how they're managed if you're looking at aggressive versus indolent diseases in general.

Lizette: So, doctor, what treatments are currently available for the aggressive subtypes of non-Hodgkin lymphoma?

Dr. Dunleavy: Yes, so as I said, the most common type of lymphoma is diffuse large B cell lymphoma; and up until recently, we have been using a treatment called R-CHOP. And over the past 30 years, different groups of investigators around the world have been trying to improve the cure rate for people with diffuse large B cell lymphoma, so they have been doing various things to do that. They've been adding drugs. They've been changing the way that they're given, etc.

About a year and a half ago, a study was published called the POLARIX Study, and this study looked at people who had a new diagnosis of diffuse large B cell lymphoma. They had a certain clinical presentation. I mentioned this IPI, or International Prognostic Index score, so everybody who went on that study had to have an IPI score of at least 2. And they were randomized to either receive the standard treatment R-CHOP or an alternative treatment called polatuzumab with R-CHP, without the O, because the O is a drug called vincristine or Oncovin®.

So, essentially, half the people received R-CHOP, half the people received polatuzumab with R-CHP. And the results showed that if you received the polatuzumab treatment, you had a progression-free survival. This is a very technical term, but basically looks at the success rate of the treatment in terms of the therapy completely eradicating the disease; and that was 6.5% higher in the group who received polatuzumab. So, that has changed the way that we treat a lot of aggressive lymphomas. The FDA approved polatuzumab for frontline treatment of diffuse large B cell lymphoma just a few months ago.

So that is really one of the big changes in treating newly diagnosed people with aggressive B cell lymphoma. There are some patients who still receive R-CHOP if they have a low IPI score. And then, and this is where it gets a bit complicated, there are other types of aggressive B cell lymphoma. There's a type called high-grade B cell lymphoma, and that's divided into two different types. One is called high-grade B cell lymphoma with MYC and BCL2 translocations, and the other type is called high-grade B cell lymphoma not otherwise specified, or NOS. Those are seen with reasonable

frequency, and we don't typically use R-CHOP type treatment for those highly aggressive lymphomas, and we use alternative regimens that are more intensive. And one of those that we use a lot of is called dose-adjusted EPOCH-rituximab. And that's also a treatment that is used in Burkitt lymphoma.

Lizette: And do you use stem cell transplantation for the aggressive types?

Dr. Dunleavy: Not in the upfront setting. So, when people are newly diagnosed with these diseases, they do not receive any kind of transplant. When diffuse large B cell lymphoma comes back, the standard in the past has been to receive further chemotherapy; and if the chemotherapy is working, then to move on to an autologous stem cell transplant.

But a few years ago, a new type of treatment for aggressive lymphoma was developed, and this treatment is called CAR T-cell therapy. So, what this therapy involves really is taking a patient's own cells and modifying them to essentially train them to attack the tumor cells. In diffuse large B cell lymphoma, there's a protein or antigen on the tumor cells called CD19, so there are now three CAR T cells approved that target CD19. And in recent studies, CAR T cells were compared to standard therapy for people who had diffuse large B cell lymphoma that came back. This was second-line treatment and, two studies, one was called the ZUMA-7 study and another one is called the TRANSFORM study, and they showed that people who got CAR T cells had a better outcome than those who got standard of care where the endpoint of the standard of care treatment was to get an autologous transplant.

So, we are now using CAR T cells frequently as second-line treatment when diffuse large B cell lymphoma comes back. And the FDA have approved them for diffuse large B-cell lymphoma if it is either not going away with primary treatment or if it comes back within a year of finishing treatment. So, we're excited about the potential for CAR T cells, and there are actually studies now using CAR T cells in the upfront setting in newly diagnosed people with aggressive B cell lymphoma.

Lizette: Wow! We do get patients asking us a lot if they can take these later treatments like a CAR T cell or a new medication earlier on in their treatment. Patients always ask us, "Why do we have to wait till second or third or fourth therapy?"

Dr. Dunleavy: Yeah. I think the results of these trials is going to be very interesting to that question, and are there certain patients with certain types of aggressive lymphomas who should get treatment like CAR T cells in the upfront setting? We will know the answers to these question in the next few years because these studies are ongoing.

The other major change in therapeutics for a lot of lymphoma patients, both diffuse large B cell lymphoma and follicular lymphoma, are the arrival of a class of drugs called the bispecific antibodies. So, these are new treatments that target two different things on B cells. There's an antigen called CD20, which most people are familiar with because rituximab targets CD20. So, the bispecific antibodies they target CD20 on B cells and then they target CD3 on T cells and this dual targeting really helps to kill the lymphoma cells.

So, over the past few years, a number of studies have been looking at the effectiveness of the bispecific antibodies both in indolent lymphomas and aggressive lymphomas. We now have a drug called mosunetuzumab which is FDA approved for follicular lymphoma. And we have two drugs, glofitamab and epcoritamab, which were very recently approved for diffuse large B-cell lymphoma. Our world is changing very rapidly, and these drugs were just approved a few weeks ago, so at our institution, we're starting to treat patients with bispecific antibodies. We're really learning a lot about the logistics of this and all of the other things that go along with having a new drug come to the clinic. So, it's a very, very complicated process, but for our patients, we're very excited that these drugs are highly effective and we're excited that we can now use them as they're approved by the FDA, so insurance companies will cover them.

Elissa: Wow! That is just so exciting. What side effects can patients expect from all of these treatments, so the bispecific antibodies, the CAR T cell, other treatments that have been used, and how are you managing those side effects to still give the patient a good quality of life?

Dr. Dunleavy: Yeah. So, with these new treatments, the CAR T cells and the bispecific antibodies, they're very, very different treatments to conventional chemotherapy, which we have been used to for a very long time and we, of course, still use all the time. They have a very different side effect profile.

One side effect that can be seen with these agents, both the CAR T cells and the bispecific antibodies, is something called cytokine release syndrome, or CRS. We are learning that that is a very important toxicity and there are things that we can do if people develop it. And if they develop a severe form of it, essentially what happens is that soon after someone receives one of these treatments, they release a lot of cytokines and they can develop symptoms from that and in the worst-case scenario, they can become very sick with it. It can cause renal failure; it can cause failure of other organs.

How we manage it is that we educate our patients about the symptoms of cytokine-release syndrome. Some of the signs that we're concerned about, if people are in that window where they might have a chance of developing it, are fever, low blood pressure, and also something called hypoxia, so people are starting to have problems with their lungs or with breathing. Those are the three signs that you might be developing cytokine release syndrome.

When our patients get one of the bispecific antibodies, we go through all of these different side effects with them, the timeline of when they might happen. When they're at home, people check their temperature a few times a day. They check their blood pressure if they have a blood pressure monitor at home and call us at a very low threshold, especially if they have a fever to get checked out.

And then, when they come to the hospital, there are a number of blood tests that we can do, and those blood tests track pretty accurately with the clinical symptoms and signs if someone is developing cytokine release syndrome. So that's one toxicity that is seen with both CAR T cells and bispecific antibodies, which is pretty new for us.

And then, another toxicity is that you can get neurotoxicity. So, with CAR T cells, a very small proportion of people can get a neurological syndrome which can be quite frightening for people if they get it, and it really constitutes a number of different symptoms and signs. Sometimes people aren't able to find words or speak for a short period of time.

But the good news is that this toxicity doesn't happen that frequently after CAR T cells. When it does happen, it is typically transient. But because of CRS and neurotoxicity, when we give CAR T cells, we like to monitor people very, very closely. I think in most centers in the US, CAR T cells are administered to inpatients and typically we tell people that they can be prepared to be in a hospital for one week after they get their CAR T cells, just to make sure they don't develop these toxicities. And if they do, then we know exactly what to do. And once that week is over, for the most part, there's no risk of those toxicities happening.

It's interesting because we're now moving towards giving these treatments outpatient, and, certainly, with the bispecific antibodies, they're very easy to administer. One of the drugs that's approved is actually a subcutaneous drug, so it's not difficult for us to administer these drugs in the clinic. And we're really figuring out ways that we can optimize assessing toxicity and making sure people are knowledgeable and they know exactly what to look for and that they will call us and will come back at a low threshold should they develop these symptoms.

Lizette: Doctor, let's discuss the future treatment for aggressive non-Hodgkin lymphomas. Are there any treatments in clinical trials or on the horizon that you're particularly excited about?

Dr. Dunleavy: Yes. Right now, I'm excited about the CAR T cells and the bispecifics. I've talked a bit about the ones that are FDA approved, but we're really moving on to another level. With CAR T cells, there now are clinical trials where more than one antigen is being targeted. Right now, the FDA approved CAR T cells just target CD19, but there are so-called bispecific CAR T cells. We're excited about those and then there are off-the-shelf CAR T cells. Everyone that gets CAR T cells, at the moment, they have to be manufactured from a patient's own blood, but there are companies that are developing CAR T cells that do not need to be manufactured from a patient's own cells.

And one challenge with giving CAR T cells is that logistically it takes some time to collect cells from someone to send them off to the facility where the CAR T cells are going to be made and then to have them be brought back again. And it can be straightforward sometimes, but I could tell you sometimes it's not straightforward. Things can happen that delay that process.

So, it's going to be really nice one day to have these therapies that we don't have to wait around for, so they're accessible to patients within two and three days, as opposed to several weeks, which is the case now. And I'm excited to see where the bispecific antibodies go just like the CAR T cells, these are also being studied in patients with newly diagnosed aggressive lymphomas. And we don't know, at this point in time, how or if they're going to change the way that we treat people with newly diagnosed aggressive lymphoma, but they may do. They work in a completely different way to conventional treatments that we have been using.

The other area that I think is really exciting is liquid biopsy. This has been something that has been ongoing in lymphoma probably for well over a decade now and there are many companies that are making assays that can detect very, very minimal amounts of lymphoma in the blood. And we now know that you can detect small amounts of lymphoma in the blood, but there now are assays where you can look at the genetic makeup of the lymphoma just from a blood test.

And I think that, in terms of projecting into the future as to how we're going to treat people in 5 years' time or 10 years' time, I think we're going to be using liquid biopsies a lot more. And we may actually be able to use information from liquid biopsies that will inform us directly on which targeted therapy is best for someone with lymphoma.

So all of that is ongoing at the moment. Most of us are not using these tests very frequently in clinic. We do use them in some people, but they're not broadly used yet, but I think that that's going to change over time, and these may replace assessment techniques like PET scans and CT scans, which while being very helpful, are problematic in that they're often positive when someone doesn't have disease. And I think people don't generally like having to go for CT scans and PET scans over and over again for several months.

I'm excited to see where that technology goes and how it's going to shape the way that we treat people. I think it's going to make it much better for patients and allow us to really give personalized treatments, which is a key theme in cancer because we understand that all these different tumors are different, but also every single person is different in the way that they metabolize drugs and the effect of X drug on 10 different people is going to be completely different. So, there are a lot of personal factors that really should be considered in the ideal world, but we're just getting to that point of personalizing medicine more and more. But it's really helpful when we're making advances, especially in technologies like liquid biopsy to, hopefully, get to that point of being able to offer people personalized medicine.

Elissa: Wow! That's just really exciting, particularly hearing about the liquid biopsy. So, our final question today. On our patient podcast homepage, we have a quote that says, "After diagnosis comes hope." What would you say to patients and caregivers to give them hope after a diagnosis of non-Hodgkin lymphoma?

Dr. Dunleavy: I would say that the treatments that we have and the treatments that we are developing are just moving at such a fast pace, that our understanding of

lymphoma is moving at such a fast pace and that is truly translating into much, much better outcomes for patients.

There are so many changes happening all the time and from the scientific perspective, identifying new pathways that are very targetable and that, just like BTK, might make a huge difference to how treatments work in a particular type of lymphoma in the future. So, there is really a lot of hope and I think it's really important to be involved in research, to support research, to access clinical trials because that's the only way that we're going to get to the next level. We have to explore these new treatments and understand them better and have scientists also discover new pathways that, at the end of the day, clinically we can target them with specific agents.

Elissa: Absolutely. Well thank you so much, Dr. Dunleavy. This was such a wonderful discussion about non-Hodgkin lymphomas and all the exciting things coming and that have just come with bispecific antibodies, the potential of liquid biopsies. I mean that's just all so incredible, and the landscape has really changed over the past few years.

And for our listeners, we will have information about our Clinical Trial Support Center. So, if you would like to look into clinical trials, as Dr. Dunleavy said, we will have information for you. But, again, thank you so much for joining us today.

Dr. Dunleavy: Yeah. And thanks to both of you so much and thanks to The Leukemia & Lymphoma Society for inviting me here today.

Elissa: And thank you to everyone listening today. *The Bloodline with LLS* is one part of the mission of The Leukemia & Lymphoma Society to improve the quality of lives of patients and their families. 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

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