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Blood Cancer United

The Bloodline with Blood Cancer United Podcast

A podcast for patients and caregivers

Episode: 'Diffuse Large B-Cell Lymphoma (DLBCL): Breaking Down and Aggressive Lymphoma'

Description:

When you hear the word "aggressive," it can feel overwhelming, but in diffuse large B-cell lymphoma (DLBCL), it can also point to something encouraging – a potential cure.

In this episode, we speak with Dr. Jonathon Cohen, of Winship Cancer Institute in Atlanta, GA, about what a DLBCL diagnosis really means, from how this common type of non-Hodgkin lymphoma is identified to current treatment options and emerging therapies. We explain what patients and families need to know about side effects. We also look at new treatments, including CAR T-cell therapy and bispecific antibodies, and the importance of open communication with your care team.

Transcript:

Elissa: Welcome to *The Bloodline* with Blood Cancer United. 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. Jonathon Cohen, a Professor of Hematology and Medical Oncology at Emory University's School of Medicine and the Lymphoma Disease Lead at the Winship Cancer Institute in Atlanta, Georgia. He is a specialist in the management of B-cell lymphomas and chronic lymphocytic leukemia,

or CLL, and leads clinical trials and other clinical research efforts at Emory and nationally. Welcome, Dr. Cohen.

Jonathon Cohen, MD, MS: Great. Thanks so much for having me.

Elissa: Well, thank you for being here with us.

So, our episode today is on diffuse large B-cell lymphoma (DLBCL), which is a type of non-Hodgkin lymphoma. Could you tell our listeners what that is?

Dr. Cohen: Sure. So, non-Hodgkin lymphoma is a type of blood cancer, and it can show up in patients in a number of different ways. And so, what I like to tell people is that, anytime I see a new patient, is that the very first thing we have to do is figure out what is it that we are treating because although lymphoma is one word, it refers to a large number of different diseases.

And so, a couple things about non-Hodgkin lymphoma in general, most people are familiar with non-Hodgkin versus Hodgkin lymphoma, but the truth is that non-Hodgkin lymphoma is about ten times as common, and it presents in a very heterogeneous or varied way. So, we have some patients that present with very rapidly enlarging lymph nodes or rapidly changing blood counts. They're in the Emergency Department or in the hospital, and that's how they have a diagnosis. And then we have other patients that come to our attention because they were getting an evaluation for some other reason. So, I've had, for example, women going for their

screening mammogram, and there's a lymph node identified that they didn't even know about; and so, many times, patients will come with no prior knowledge or no symptoms at all.

And so, part of what we like to do, or what we need to do, is to first figure out what is the entity that we're talking about. Now, I typically think of non-Hodgkin lymphoma as being divided into two primary buckets. There's the aggressive non-Hodgkin lymphomas and the nonaggressive or indolent non-Hodgkin lymphomas; and even within those buckets, there can be a lot of variability.

Now, diffuse large B-cell lymphoma is the most common type of aggressive non-Hodgkin lymphoma that we see; and so typically these are patients that often notice that they're having some enlarged lymph nodes, they might be having some other symptoms, like unexplained fevers, weight loss, difficulty eating or drinking, and otherwise may feel ill. They may not be acutely sick in the hospital but have noticed that something has changed, and that's often how they come to our attention.

Elissa: So, how is diffuse large B-cell lymphoma different than other types of non-Hodgkin lymphoma, besides being aggressive versus the more indolent or slow-growing types?

Dr. Cohen: Yes, so diffuse large B-cell lymphoma is, as I mentioned, the most common subtype of lymphoma. But it is distinct from other types that we see in its clinical

behavior as well as the way it looks under the microscope and the way it may behave when we look at it in scans and so forth.

So, typically when we look under the microscope, we see a bunch of abnormal-appearing B cells that the hematopathologist identifies; and they can do a number of different stains and other tests, which help to distinguish this from other types of lymphomas and other types of cancers. And then clinically, when I see somebody that comes to see me, these are patients that typically will have lymph nodes that we can feel, either in their neck, under their arms, or perhaps in their groin. And again, they may have other symptoms that are showing up.

At the end of the day, although the symptoms and the clinical presentation is really important, without that accurate diagnosis by the hematopathologist, it can be difficult to really narrow down the specific subtype. But, when we have a patient with the right symptoms as well as the right diagnosis by pathology, that's typically how we make the diagnosis.

Lizette: So, before we get to the current treatments, with DLBCL being considered an aggressive lymphoma, is the goal of treatment cure?

Dr. Cohen: Yes, so it's a great question. So, anytime we see a new patient, once we've made the diagnosis, the next question that a lot of people have is, "Well, what does that mean for me? What can I expect down the road?"

And, fortunately, in general, with non-Hodgkin lymphomas, although it is a serious disease it's a cancer of the blood, we have success in treating a variety of different lymphoma subtypes. And so, it's very important when you first are going over the diagnosis and coming up with a treatment plan to have an understanding of what to expect down the road.

Now, with diffuse large B-cell lymphoma, even though it is an aggressive lymphoma and people often hear the word aggressive, and that certainly doesn't sound like a positive, we know that the aggressive lymphomas are also the more curable lymphomas. And so, when I meet a new patient who has diffuse large B-cell lymphoma, the first thing that I'm discussing with them is that in most cases our goal is going to be to cure them of the disease. And I think it's important for people to recognize that from the get-go. It's a little bit different than other types of lymphoma where we might not necessarily be able to cure those patients but can manage that disease as more of a chronic illness. And so, it's an important distinction to make early on so that patients have a good understanding of what to expect.

Lizette: So, these slow-growing types, the indolent types, they're the ones that are more chronic in nature; so, it's really not cure for that type. It's really right now quality of life and management of the disease?

Dr. Cohen: That's correct, although I think it's important to recognize that even though a low-grade lymphoma may or may not be curable, many of those patients will

live a normal life expectancy. And to be honest, a large part of what I'm trying to do when I'm managing a patient in that scenario is making sure that they're keeping up with all their other healthcare needs, whether it's screening for other cancers, whether it is making sure that they're taking care of their heart health and so forth because in most cases those patients will pass away well down the road from something unrelated to their lymphoma.

For the aggressive lymphomas like diffuse large B-cell lymphoma, it's a little bit different. Those are patients where if we don't do something right away, they can start to become quite ill and start to have symptoms; and it can develop into more of a life-altering or life-threatening situation. But with therapies that we currently have, if we identify those patients and get them started on therapy quickly, most of them will respond; and the majority of them will not have to get any treatment again.

Lizette: Okay, and I'm meeting more and more younger patients, so I thought that diffuse large B-cell lymphoma was more for patients that are more advanced in age. But it could be for different ages, correct?

Dr. Cohen: Yes, that's correct. And so, I think it also raises a number of important points that we need to think about. So, historically, I had thought about diffuse large B-cell lymphoma, to your point, as being a disease that people got usually in their 60s or 70s, maybe in their 50s. But we definitely do see patients that develop the disease earlier. I've had patients in their 20s and 30s even, and this raises important

considerations like fertility and future fertility. Occasionally, we have patients that are actually diagnosed during pregnancy; and these are also patients that are often in a different career stage and life stage. So, they may have young children at home, they may be just getting their career going, and now all of a sudden we're having to embark on a course of treatment that they weren't planning on. So, I think that's a really important point; and there's a lot of work being done to try to better understand the experience and the optimal therapies and supportive therapies for our young adults.

Elissa: Now, we'll talk about side effects a little bit later in the discussion. But, with patients getting diagnosed at a younger age, is there also a concern for the number of years that they have left, with decades left and dealing with potential side effects, long-term or late-term side effects?

Dr. Cohen: Yeah, I think that's a really important point to discuss. So, if you have somebody, for example, who's in their mid-30s and who's diagnosed, obviously, the first order of business for an aggressive lymphoma is to try to put them into remission and, hopefully, have them be cured of the disease. But you're exactly right that there is, hopefully, another 50 years or so, if not more, of life ahead of them. And so, those are patients that do require ongoing counseling and monitoring. So, we know, for example, that patients who have had one form of cancer are at increased risk for developing other forms of cancer. So, it's very important that those patients have close follow-up with their primary care doctor, that they are having all age-

appropriate cancer screening, that they're managing other potential comorbidities or other medical conditions that come up.

Specific to the treatment, those patients, especially young women who have had to have radiation as part of their therapy, can be at risk for the development of breast cancer. All patients who have had radiation therapy to the chest can be at risk for cardiovascular complications. Fortunately, these are not common; but they do require ongoing follow-up.

And then, in general, patients that have been on chemotherapy can have subsequent bone marrow conditions and other complicating issues that arise down the road. And so, while our goal is to cure patients and while many of them will be cured and go onto thankfully life a normal life, it is important that they recognize that they've had this event, that they maintain follow-up. And with young people, especially, they tend to be more mobile. They tend to move for a career, move for family reasons; and so, it is important that even if they move to a new location, that they establish a connection with an oncologist wherever they go just so that if anything does pop up, they have somebody that can help support them.

Elissa: Yes, that is very good advice. Now, let's get into the current treatments for diffuse large B-cell lymphoma. What are they?

Dr. Cohen: So, for the typical patient that comes in that's newly diagnosed, at present, our typical treatment combines immunotherapies as well as traditional chemotherapy. And so, I think it's important to highlight that although there's been a lot of discussion in other settings about getting rid of chemotherapy, and that may be something that one day we get to with this disease, currently, the optimal way or the best way we know to treat and cure a patient is a combination of chemotherapy with immunotherapy like a monoclonal antibody.

Now, there are, I would say, for typical diffuse large B-cell lymphoma, there are two primary regimens that we use. These are both given once every three weeks. They're both given as an outpatient, and in most cases, we give for a total of six cycles.

There are some differences and reasons we might choose one over the other. There was a large trial that many of the listeners may be familiar with called the POLARIX trial, which compared our long-term standard of R-CHOP with a modified version, which included a new therapy called polatuzumab vedotin, and we call that Pola-R-CHP. And there's some nuance to why we might choose one over the other, but I think it's important anybody that's diagnosed with diffuse large B-cell lymphoma that's considering their initial therapy, that they, at least, have a conversation with their doctor about which of those two approaches might be more appropriate for them.

Now, for patients that are older or have other medical conditions or have underlying heart failure or other things that may make it difficult for them to receive the standard

treatment, there are other options. There's lower-dose therapies, and so it's always important to recognize that just because a patient may not necessarily be in a position to receive the full-dose standard treatment, that there often are still therapies that can be very effective for them.

Elissa: That is good to know. So, what about stem cell transplant? Since you're looking for a cure, is that something that's a possibility for diffuse large B-cell patients?

Dr. Cohen: So, in general, stem cell transplantation is used in patients with diffuse large B-cell lymphoma; however, it is almost exclusively used in patients who have a recurrence of their disease. And so, there was a time where we were thinking that, well, perhaps if patients, especially if they have higher-risk disease or more aggressive-behaving disease, maybe we get them into remission. And to really try to maximize the likelihood of cure, we could then follow that up immediately with a stem cell transplant.

And just so folks are aware that may not understand some of the nuances of transplant, there are two primary types of transplant that we use. One is called an autologous stem cell transplant, and this is a scenario where we collect somebody's stem cells. And then we administer a very, very high dose of chemotherapy that's designed to really wipe out any residual lymphoma; and then we rescue their bone marrow. We allow them to recover by giving them the stem cells back. And then the

other type of stem cell transplant that is used is what's called an allogeneic or a donor transplant, and that's where we'll use somebody else's stem cells to actually try to attack the lymphoma.

Now, although these are both called transplant, and there's some similarities, the way that they attack the lymphoma are very different. So, whereas with autologous transplant, we're trying to give a very, very high dose of chemotherapy to wipe out any residual disease, with the allogeneic transplant, we're hoping that a donor's immune system might be able to come in and help attack the lymphoma.

And each of these have their own complications and risks associated with them. And so, the reason I bring this up is that it's important to recognize that a stem cell transplant, when and if that ultimately is an appropriate option for a patient, it's important to identify which specific type of transplant is most appropriate for a given situation and to understand that it's a big deal. It's a several-week process. Frequently, you're in the hospital for several weeks. And if you're using donor stem cells, there's a number of medications that you have to take to suppress your immune system for an extended period of time.

So, getting back to your question about when would we think about doing a stem cell transplant, despite the risks associated with it, there was a hope that, perhaps, patients that had highly aggressive disease, high-risk disease might benefit from that extra treatment. But unfortunately, we found that there was not a significant

improvement for the majority of patients with a stem cell transplant after their initial therapy. So, in almost all cases, if a patient goes through treatment and they go into remission, they're off therapy at that point and we go into observation.

Now, in the relapsed setting, there are reasons that we might think about a stem cell transplant. And really for about 20 to 25 years, that was our standard. Anybody that had recurrent disease that was eligible, we would try to take them to an autologous stem cell transplant.

And in the last several years, there's been a handful of studies that have come out looking at a stem cell transplant versus a different type of cellular therapy called chimeric antigen receptor T therapy or CAR T therapy. And in some instances, the CAR T is a better option for patients, especially if they've had an earlier recurrence, whereas for other patients, we might think about an autologous transplant.

The most important thing, I think, for patients to understand is that if you find yourself in a situation where your disease has come back and you're having to have a conversation about additional therapy, it's important to bring up the question about transplant or CAR T and make sure that you, at least, have the opportunity to be evaluated by a physician with expertise in those cellular therapies who can help determine whether one of them may be a good option for you and whether you would be medically suitable to move forward.

Elissa: So, CAR T-cell therapy is approved for diffuse large B-cell lymphoma?

Dr. Cohen: Correct. So, CAR T-cell therapy is approved in patients in both second line and third line, and there's some nuance to why we might choose it in one line versus the other. Just in general, patients who have a recurrence within the first year of treatment, that's one of the primary indications for patients in the second line. And so, if I have somebody who completes therapy but has recurrent disease fairly early on, I'm going to be thinking about CAR T for that patient.

In addition, we know that the criteria to be able to safely get through CAR T are different than the criteria for a stem cell transplant. And, in fact, many patients who might not be the best candidate for a transplant may be an excellent candidate for CAR T. And in those patients, also, there's an approval. So, folks who are not felt to be a candidate for stem cell transplant can potentially move forward with CAR T.

Elissa: What about bispecifics? So, on that same line of that T-cell therapy. Are they approved for diffuse large B-cell?

Dr. Cohen: Yes, so in the last couple of years, we also now have approval of bispecific antibodies; and these are therapies where you have an antibody that has sort of two targets. One is CD20, which is the marker for the B cells that make up the lymphoma. And then they have another target which are the T cells, and the idea is that they bring the T cells in close proximity and sort of engage them with the B cells to try to facilitate

the elimination of the lymphoma. It's a very exciting new group of treatments, and I would say that at present, it is very much in flux how best to use them, when to use them, and so forth.

Currently, I think about these in patients who have had two prior lines of therapy and who are needing some additional treatment, whether that be after CAR T or transplant or after other therapies. But there's a lot of data coming out looking at their use earlier on. And, in fact, there are studies going on looking at the use of them as part of the frontline or first line of treatment. And so, as I mentioned before, right now we're still looking at combination chemotherapy; but with bispecific antibodies and other therapies that are being evaluated, I wouldn't be surprised if in the coming years, we're using less and less chemotherapy in the frontline. But that still is a little ways away but very exciting new group, of therapies.

Lizette: So, are they approved right now for second line or third line for diffuse large B-cell?

Dr. Cohen: For the bispecific antibodies, most commonly I'm thinking of them as a third-line regimen. There are sometimes I might try to use them in the second line, depending on what's going on with an individual patient. I think it's important anytime somebody has recurrent disease that they have a discussion with their doctor about the treatment options, whether some of these newer immunotherapies could be

something that's considered because there are times we might think about them a little bit earlier on.

In my own practice, I would say all things being equal, I typically am looking at CAR T versus transplant as my second-line approach and then thinking about bispecifics as a third line in most cases.

Lizette: And I know that our patients keep hearing different terms like bispecific or BiTE. Those are the same thing?

Dr. Cohen: So, I would say for all intents and purposes, they're typically used interchangeably, which, I know, can be challenging. So, BiTE refers to something that's called a bispecific T-cell engager. But the molecule that is used is really an antibody that sort of targets two different targets. So, I think, although not optimal to have all these different terms floating around, and I know some that my scientist friends would probably cringe. At least in my own practice, often think of them as being more or less interchangeable from the clinical perspective.

Lizette: And those are also treatments that are given outpatient. I know that some are subcutaneous.

Dr. Cohen: Correct, correct. So, the actual administration of a bispecific or BiTE is pretty straightforward. There are subcutaneous formulations. There's some that are given by IV that are moving towards subcutaneous. So, the actual administration is

pretty straightforward. You may have heard or patients may have heard in the past or their physicians may recall that not too long ago many times patients would be admitted, not for the actual administration, but for monitoring afterwards. And this is because during the first couple doses, especially as you're getting somebody up to the full dose, there can be some toxicities that can be difficult to manage at home. These are called cytokine release syndrome or CRS, as well as some neurologic toxicities.

These are very similar to what we see with CAR T, although, fortunately in lymphoma-directed bispecifics, the incidence and the severity are lower. So, fortunately, most patients will do just fine. But if you have a patient that does develop a fever, does have low blood pressure, high heart rate, or other symptoms while they're at home and they've started a bispecific, it's very important that they seek immediate medical attention. And there are specific therapies that we use.

Unfortunately, these therapies that we use and sort of the ability to rapidly evaluate somebody is not necessarily available at every site, every place, at all hours of the day and night. And so, that's why, at least at present, most of the places where folks are receiving the bispecifics, especially at the beginning, are at some of our larger centers where they do have the resources in place to manage these complications if they occur.

Lizette: Okay. And I know we're going to get into a conversation now about side effects and if they're manageable. So, a lot of our patients are looking into newer

therapies and what's new because they're also looking for therapies that have less potential side effects. So, are the new therapies that you're talking about potentially have less side effects for folks?

Dr. Cohen: So, it's a great question. I think that it's important to try to highlight that, number one, any therapy that we use has the potential for side effects. And so sometimes when people hear, "Oh, this is chemo-free or we're moving away from chemotherapy," that it means that the therapies are going to, by default, be safer and easier. And many times that is true. Many of our newer therapies don't have some of the same real challenging side effects that we used to deal with before. So, nausea and vomiting, for example, is not as commonly an issue for some of our newer immunotherapies.

We don't necessarily have patients whose blood counts are going all the way down to where they're needing transfusions and where their white blood cells are really bottoming out, like we do with traditional chemotherapy. Typically, there's not the same hair loss and other things that can happen. So, in that regard, it is true that, as we move away from chemotherapy and as we look at some of these newer treatments that are coming out, we're not seeing that quite as much, as we would with traditional chemotherapy.

But it is important to highlight that these patients can still experience immune side effects like the CRS, like the neurologic toxicity. And with the bispecific antibodies in

particular, there can be some unusual infections that occur that we don't always see with more traditional chemotherapy. And so, it's important that patients are being monitored and that they still recognize that there are things that can emerge that would need to be dealt with. So, it's not totally free of side effects.

Lizette: Yeah. And at this point, because we know about a lot of the side effects, as a physician, you're being proactive too with your patients in regards to managing those side effects.

Dr. Cohen: Correct. So, absolutely. And the only thing I would say to sort of add to that is that, yes, I have a conversation with my patients and their families about what to expect. But it also highlights the importance of having a team of people that are helping to care for every patient. And so, for me, at my center, that includes a nurse practitioner that I work with an oncology-trained nurse; a pharmacist; social workers. There's a whole team of people that are involved with helping to manage side effects or helping to prevent side effects, and I can't tell you how frequently I walk out of a room and go grab my pharmacist who has oncology training and say, "Hey, this patient's experienced this and this. Does this sound like it's something you might expect from the treatment?" Because people often think that, as the physician, that we know everything that's going to happen and we have a full awareness of all the nuances that can occur. And the truth is we really do rely, not only on our own

experience and our own knowledge, but on the knowledge of our team members who can help us.

And I also think it's important that people realize that if they call in with an issue and speak with one of the nurses in our clinic, that very commonly those are nurses that are familiar with the medications that are being used and can help triage whether somebody needs to be seen right away, could they be seen the next day, or is this something that is to be expected and they can manage it at home safely.

So, absolutely. We take this very seriously. We encourage our patients to contact us if they're having anything pop up that seems out of the ordinary. And we really do rely on a team of experts to help make sure that patients are receiving therapy safely.

Lizette: Yeah, I'm glad you said that because sometimes patients have expressed to us that they may not feel comfortable speaking about side effects potentially because they feel that the therapy is working. So, if they talk to you about side effects, that maybe something will change.

Dr. Cohen: Yeah. That's a very common concern that people have. And one of the things that I try to talk with patients about is that there's a lot that goes into a decision to adjust or hold a treatment or to stop a treatment. And that in almost all cases, it is not a unilateral decision where they're going to make one comment and then the whole thing stops.

So, I think, a couple things that at least, keep in mind and this goes back to some of our discussion from before, is what is the goal of the therapy? So, if I'm trying to cure somebody of their lymphoma, and that's our goal from the beginning, then maybe you tolerate a little bit more side effects, a little bit more toxicity because, if you can get through this, then there's a reasonable chance that patient may not have to go on therapy again.

On the other hand, if you're treating a patient for whom cure may or may not be as realistic or it's a lower-grade lymphoma or for whatever reason, that's not necessarily the focus, in my mind the goal is to try to maintain their patient's quality of life and to maintain control of the disease for as long as possible.

And so if that means that maybe I need to spread out a treatment from every three weeks to every four weeks or I need to lower the dose a little bit, I would much rather do that and keep them on the treatment that's working for them than push it; and then all of a sudden, another month down the road, we have to stop it entirely because they're developing some sort of disabling complication.

And so, I think it's very important that patients speak honestly with their physician because, again, as long as we know that something's happening, often we can either manage it by tweaking the regimen, as opposed to having to stop it entirely. There might be medications that we can use. There's any number of things that we can do. But if we don't know about it, and then all of a sudden things come to a head in a

crisis-type situation, then there are times when we have to stop the treatment altogether, which is not ideal if it's working.

Elissa: Now, with this being a B-cell malignancy, is there also a level of being immunocompromised throughout or after the treatment, including with maybe their immunity to vaccine-preventable diseases that they might have had a prior vaccine to?

Dr. Cohen: Yes. So, we know that patients that have a B-cell malignancy, even before they start therapy, the general thought is that they probably already have some degree of immune compromise.

Now, one of the things that can be very challenging in my own clinic and for patients is the recognition that this is not a binary thing that, you're either immune compromised or you're not, that it really is a spectrum. And at least in my own clinic, I have patients all the way from, maybe if we did a very specific lab testing, we could identify some areas of compromise. But otherwise, they're functionally able to be in the world without too many extra precautions, all the way to people that have had a stem cell transplant that really almost pretty much need to be isolated for an extended period of time. And there's a whole spectrum in between.

So, the first thing I like to tell patients is, yes, there's probably some degree of immune compromise, but that does not mean that you have to entirely shut down your life. It

does not mean that you can't see your family and friends. It may just mean that you need to be more thoughtful in how you do that. Maybe instead of going out to dinner on a Saturday night when everybody's crowded waiting for a table. You go a little bit earlier in the day or something like that.

We also recognize that the type of treatment that a patient receives, the duration of therapy, the number of lines of treatment that they've had, any number of other factors could come into play when determining somebody's degree of immune compromise. And so, we do our best to highlight to patients when we think they're at the highest risk and when is the time for them to maybe abstain from, trips or other things that they have control over.

The other thing though that I'll tell people is that once-in-a-lifetime experiences like a wedding or a funeral or something that is not just something that you can postpone for six months, something that comes up that is important and is only a one-time thing, we can almost always make that work safely. And so, it's very rare that I would tell somebody they can't attend something like that; but they may just need to do it in a different way.

To answer your other question about the duration of therapy and sort of what that means for other illnesses that they could get, we know that, in general, both your vaccine response while you're on therapy and likely your immunity to some prior vaccine-related illnesses can wane somewhat. I always tell people though that I don't

want folks to be nervous. I've never had a case of diphtheria. I've never had a case of polio. So, it's not that people are just coming in routinely with these sorts of issues, but it's important to recognize that especially if you're around young children that may not have been vaccinated yet, or you're in an area where there is an outbreak of measles or other things to be cognizant of the fact that your immunity may not be quite as strong as it was before. And, again, it doesn't mean you can't go out. It just means that you want to be aware of that.

Elissa: That is good to know.

So, let's talk about the future of treatment for diffuse large B-cell lymphoma. Are there any emerging therapies or those in clinical trials that you're particularly excited about?

Dr. Cohen: So, it's interesting because we are just now sort of coming out of an era where there was a number of new therapies that were approved. So, in addition to the bispecific well the CAR T and then the bispecific antibodies, there are some antibody drug conjugates. There's a drug called, for example, loncastuximab tesirine, or Lonca-T, which is an antibody drug conjugate that targets CD19. There was another antibody called tafasitamab that we combine with an oral therapy called lenalidomide. So, a number of new therapies.

And, in fact, there's another therapy called brentuximab vedotin, which has been approved for Hodgkin lymphoma for a long time and for which we really thought there was no role in non-Hodgkin lymphoma. But there was a nice large study that was done that highlighted the fact that when combined with other therapies, it can add significant benefit.

And so, there's a wide range of new therapies that are coming out, and in most cases when I see a patient with recurrent disease especially, we're not necessarily jumping right to chemotherapy. We have these other approaches.

I think what now is particularly exciting is that we have these therapies. We're getting more experience with them, but we're also starting to combine them. And that's really leading to some really impressive results, some really deep remissions, long-lasting remissions. And whereas in the past, the thought was, well, if somebody has recurrent disease and we're going to try to cure them, they either need to get a stem cell transplant or they need to go to CAR T. And that still is true, that those are patients that we can potentially cure. But we're seeing with some of these combinations of novel therapies patients are still experiencing very long remissions, some of which are still ongoing. And so, it's a very exciting time.

I think the other area where there's a lot of interest is trying to expand on our repertoire of cellular therapies, either looking at newer targets or newer cell types. And these, hopefully, will allow us to have better targets and have better efficacy but also maybe

a little bit safer. There's interest in looking at CAR T-cell therapies what we call, off-the-shelf. So, instead of having to collect your T cells, send it off for manufacturing and bring it back, that we might be able to use T cells that are sort of already available for you.

So, a wide range of novel things that are currently available and that are coming down the pike. And so it's a very exciting time and for me, at least, to be managing patients with diffuse large B-cell lymphoma because in the not-too-distant past, if you had a patient who received a stem cell transplant and the disease came back or they weren't a candidate for a stem cell transplant, there were very limited options that you could feel good about offering. And, fortunately, now, we're in a new era where many of these are very highly effective, patients can continue to work, they can continue to live their lives and frequently are having prolonged control of their disease.

Elissa: That is so very exciting. And you mentioned earlier that I believe they're also looking into moving some of these therapies more into the frontline as well?

Dr. Cohen: That's correct. So, there's trials ongoing now looking at many of these therapies in the frontline. Many of the initial data looked really good. I think it's important to recognize, though, that we'll want to not only show that the data looked good and that patients are responding but that they're actually doing at least as well if not better than patients who are getting our standard treatment. And so, we're not quite at that place yet where we're ready to roll these out outside of the setting of a

clinical trial. But if you are in a place where you have access to a clinical trial and that's using some of these newer therapies, I would certainly encourage you to consider it because it's very exciting; and, if I had a crystal ball and, you know, looking five to ten years down the road, I think it's highly likely that many of these therapies that have recently come out and that we're using in the relapse setting will likely find their way to the frontline.

Elissa: Yes, definitely. It is always important to encourage patients to look into clinical trials and see if they might be able to get on a trial with a novel therapy or, again, moving it towards a frontline therapy. And we will have information in the show notes about our Clinical Trial Support Center for patients who would like to look into clinical trials at any point after their diagnosis.

So, thank you so much, Dr. Cohen, for joining us today and telling us all about the current treatments and news with the emerging therapies and those in clinical trials. It is a really exciting time for blood cancer research where so many new things are coming out and giving many more options to patients who may have relapsed or not responded to treatments. So, that is wonderful. And so again, thank you so very much for being here with us today.

Dr. Cohen: My pleasure, and I would just add a shoutout to thank you and Blood Cancer United for all the work that you're doing to support patients. I can't tell you how many patients I see in clinic who have utilized the resources that are available,

and it's really made a big difference for them. So, I'm very happy to be here with you today.

Elissa: Thank you so very much.

And thank you to everyone listening today. *The Bloodline with Blood Cancer United* is one part of our mission to improve the quality of lives of patients and their families.

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In addition to the Lounge, we could use your feedback to help us continue to provide 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 Blood Cancer United staff, please email, TheBloodline@bloodcancerunited.org. We hope this podcast helped you today. Stay

tuned for more information on the resources that Blood Cancer United 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? Blood Cancer United 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 BloodCancerUnited.org/PatientSupport. You can find more information on diffuse large B-cell lymphoma at BloodCancerUnited.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.