LEUKEMIA & LYMPHOMA SOCIETY®

THE BLOODLINE WITH LLS

A PODCAST FOR PATIENTS AND CAREGIVERS

Episode: 'Immune System To The Rescue: Immunotherapies In Blood Cancer'

Description:

Please join us as we speak to Dr. John Leonard of Weill Cornell Medicine. In this episode, Dr. Leonard discusses the broad array of immunotherapy treatments, in which a patient's own immune system is stimulated to fight cancer cells.

From CAR T-cell therapy to monoclonal antibodies to new bispecific therapies, Dr. Leonard shares how these immunotherapies are changing the landscape of cancer treatment and giving hope to more blood cancer patients.

Transcript:

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

Jesse: I'm Jesse.

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

Elissa: Today we will be speaking to Dr. John Leonard, a Professor of Hematology & Medical Oncology and Assistant Associate Dean for Innovation and Initiatives at Weill Cornell Medicine in New York. He is also the Executive Vice Chairman of the Weill Department of Medicine and New York Presbyterian Hospital where he is an attending physician.

Dr. Leonard also serves as the Chair of the Lymphoma Committee of the Alliance for Clinical Trials in Oncology. Dr. Leonard's primary research interest is in the development of novel therapeutic strategies for the treatment of lymphoma and related hematologic malignancies. Much of his work has involved the development of

novel therapies for lymphoma, including monoclonal antibodies, other immune-based treatments, targeted agents, and other innovative approaches.

If you're a long-time listener of *The Bloodline*, you may recognize Dr. Leonard from a September 2017 episode titled, "Diagnosed with Diffuse Large B-cell Lymphoma: Now What?" where he shared the latest advances in lymphoma treatments. Welcome back to *The Bloodline with LLS*, Dr. Leonard.

John P. Leonard, MD: Thanks very much for having me. It's great to be here today with all of you.

Elissa: Wonderful. So, let's get started by learning again a little bit about you. How did you start in the field of medicine and then studying blood cancer?

Dr. Leonard: I always was interested in science. I thought that medicine was a great way to combine a scientific interest with helping people. And once I got further into medicine, I had some early research experiences in blood cancer, really just kind of randomly had an opportunity to work with an investigator while I was in college that happened to focus in blood cancer. So that started me off in this area.

But really, I felt like cancer research over my professional lifetime would really be an area where there would be tremendous amount of progress. And so, I thought it would really be exciting to work in an area that had a big upslope of the curve where there was a lot of progress happening, more likely to be happening, and to be a part of that.

And thankfully, this really has been an area where there's been a tremendous amount of progress. It's been fun to be a small part of it; and really immunotherapy is one huge aspect of that, so it's great to talk about that area with you today.

Lizette: Yeah, definitely. I think during your career, you have seen a lot of advancement for our blood cancers; and like you just said, immunotherapy is one of those advancements.

This podcast today is on immunotherapy. Can you just let us know, and the folks listening, what immunotherapy is?

Dr. Leonard: That's a big topic. Really, we know that cancers and blood cancers occur, in a host or in the patient, or in the case of, obviously, patients with blood cancers. And all of us have an immune system that helps to fight off infections.

But we also know that our immune system does a lot of different jobs in fighting off cancers and tumors. Some would argue that at some level we may very well get little, tiny cancers or bad cells occurring in our body all the time, but our immune system gets rid of them. And so the concept that the immune system is potentially valuable in getting rid of cancers and blood cancers as well, and when tumors actually occur to the point that they manifest themself in a person where you see a lump or you see abnormal blood counts or whatever the tumor shows itself as, by definition, that tumor has acquired some ability to evade the immune system.

And so the concept of immunotherapy is to say, well, if we think that tumors happen all the time, but 99.9% of the time our immune system can deal with it and get rid of it before we even see that it's there and, in fact, in those cases it never even occurs or becomes visible to us because the security guards, so to speak, get rid of it, why is it that the 0.0001% of the time when the immune system can't do the job, why is it that the immune system can't do the job? What about the immune system or what about those tumor cells that allow them to escape the immune system; and, therefore, what can we do to help the immune system to essentially beef up its ability to fight off the tumor cells when they occur?

And so, the concept of immunotherapies is really a broad array of types of treatments that, in a nutshell, stimulate the immune system to fight the tumor cells. These can be manifested in a number of different ways. Some of the earliest immunotherapies were what we call cytokines, were kind of chemicals that are made by the immune system to fight invaders.

So, for instance, when you get the flu or when you get an infection, your immune system makes various chemicals that help the immune system to fight off that infection. Some of those chemicals make you feel crummy, like when you get the flu, you get a fever and other side effects. And so, some of these immunotherapies, at the most basic sense, can cause symptoms like having an infection, things like fever and aches and pains. That's one broad category that broadly stimulate the immune system and our immunotherapy. So, a drug called interferon, which used to be used more commonly in certain types of blood cancers, less commonly now, is one example of an early immunotherapy.

Then we have immune treatments or immunotherapies that are antibodies or immune proteins that, instead of being made by your immune system to fight an infection, like if you get the flu shot, you make antibodies against the flu virus. These are antibodies that are directed against the tumor cells to help fight the tumor cell. And so, an example would be a drug like rituximab or Rituxan®, which has been used for almost 25 years now to treat certain types of lymphoma. There are other examples of immune therapies that fall into the antibody category.

There are other antibodies that are widely used, that are immunotherapies, that are in the category of immune checkpoint inhibitors. These are drugs like nivolumab, pembrolizumab, that are approved in the blood cancer world in Hodgkin lymphoma, as an example. But they're also used for various solid tumors, such as melanoma and many others.

These are antibodies that can essentially help the immune system overcome some of these, what we call checkpoints. So, if you think about tumor cells having a shield that protect them from the immune system, these immune checkpoint inhibitors remove the shield and essentially allow the immune system to go after the tumor cells. So that's another category of immunotherapies.

And then we have a variety of antibody drug conjugates, basically immune proteins that deliver drugs, more specifically, to tumor cells. That's another form of immunotherapy. And then we've gotten much into the category of bispecific antibodies, another area that's coming onto the scene that works in an antibody and immune protein that binds a tumor cell with one arm and an immune cell in another arm and brings them together so the immune system can be activated.

And then finally, we have a large category of immunotherapies that are in the family of what we call CAR T cells. T cells are immune cells that are naturally occurring in our body to fight infections. But in the case of blood cancer therapy, they are removed from the individual, like a fancy blood donation, engineered to better fight the tumor cells, given back to the patient to fight the tumor cells, and can have very dramatic effects in certain types of tumors.

And so these are kind of the broad categories of immunotherapies that are actually making a difference for our patients. But you can see that this whole area of work is really quite broad and affects and impacts many patients when these drugs are given by themselves, when they're given in combination with other drugs, and really making a huge difference for patients broadly.

Elissa: That's great. It's really interesting to hear how we're using a patient's body to fight their own cancer. I mean that's really just the whole base around this, correct?

Dr. Leonard: For the most part, it does rely on the patient's immune system. Certain patients with leukemia may be familiar with the allogeneic stem cell transplant, when patients get chemotherapy and then get stem cells which are, in part, immune cells from another person, that are essentially, given to the person as part of an allogeneic stem cell transplant. And that is relying on this other person's immune system to help fight the blood cancer.

But for the most part, that is a relatively narrow setting of immunotherapy where the immune activity is coming from someone else. For the most part, this is really relying

on the patient's immune system to do the job. For some reason, the tumor has properties, or the patient has properties that the immune system can't do the job, so it's essentially figuring out how can we rev up the immune system to help it do the job; and so the patient's own defenses can actually do the job better in a way that makes a difference against the cancer.

Elissa: Wow, that's amazing. Now, you mentioned that cytokine is not recent. That's been used for a while, and we've really been starting to hear a lot about CAR T-cell therapy quite a lot recently. What are the other ones that are just very new on the market or coming out?

Dr. Leonard: So, I think that there have been antibodies of various forms. Antibodies are immune proteins that basically are engineered to go after a specific target. So normally our body has antibodies or immune proteins that are floating around, made by our immune system to fight infections, and they really are very broad. They go after a broad array of infections, and our immune system is engineered so that when new infections or new things come into our system that we need to get rid of, our immune system is very good at creating new immune reactions to get rid of new things that come about.

So, for instance, COVID wasn't around for a while; but our immune system is now adaptable to react to that and make immune responses to COVID, even though, five years ago that didn't exist. But our immune system can adapt and respond to new invaders so to speak, much like an army can, to some degree, adapt to new challenges and new invaders that it might have to deal with.

There are a number of different antibodies being one arm of the immune system. These have been used for a variety of different settings. I think the newer areas include things like the bispecific antibodies, which are, again, these immune proteins that can in one arm, target the tumor cell and in another arm, activate the immune system in a very effective way.

So, these are really new, and they are most active so far in lymphoma and in multiple myeloma. There has been a version of one of these called a BiTE or a bispecific T-cell engager, and this is one that has been available and around for really a few years in acute lymphocytic leukemia.

Elissa: I'm curious about these antibodies because we've heard a lot, certainly, during COVID about these monoclonal antibodies; and then you're discussing bispecific antibodies. Are these things that are manufactured or is it more like what we're hearing with the COVID vaccine, where you get the injection of the mRNA or whatever it is, and then our body is making the antibodies. How does that work?

Dr. Leonard: So, in a vaccination strategy like in COVID, or a flu shot for that matter, you basically get a vaccine with essentially a piece of, or the vaccine in the case of COVID, generates a piece of a target on the virus that helps the immune system then go after that target when it sees it after an infection from the virus.

Cancer vaccines have been studied in many different settings. They've been studied in lymphoma and leukemia. They've not really panned out in that way in part because the immune system reaction to the extent that a vaccine can work in cancer has been fairly limited. The immune system just hasn't been strong enough.

So, in the CAR T cell setting, it's really the idea that the T cells are there. They may be impacted or weakened by prior treatments that the patient had that suppressed the immune system or the tumor may just have some sort of inherent resistance to the immune system.

And so, the idea, for instance, for a CAR T cell is that the T cells are taken out of the patient. They are genetically modified so that they are more active and that they go after a target on the tumor cell that's been specially selected. And then they're given back to the patient, usually with some light chemotherapy to make space for the CAR T cells to be able to grow and to multiply and to go do their job. And then the idea is that that can be very effective.

So by definition, the immune system needs some help here, and we're really relying on tricks to make the immune system stronger or to really give the immune system a helping hand to be able to go after the tumor cell or in some scenarios, more so in the research setting, it's how can we make the tumor cell more obvious to the immune system so that it is more sensitive to what the immune system has to go after.

Jesse: You mentioned that immunotherapies can be used by themselves or in combination with another therapy? Does the type of blood cancer dictate whether it's used alone or not?

Dr. Leonard: I think that the idea that the immunotherapy can be used in combination is really an important one. Normally most drugs are developed by themselves because we kind of figure out does the drug work. Does it have activity against the tumor cell? What are the side effects of the drug? Depending on what all that looks like, it may be that a drug is approved by itself as a first step in the process.

And then if that happens, so, for instance, rituximab, an antibody, the bispecific antibodies, the CAR T cells, or the immune checkpoint inhibitors that we've talked about, all of those have largely been approved in most settings by themselves as a single agent.

And then the next step is how do we make them work even better because, so far, in almost all of those settings, they have not gotten rid of the tumor entirely. One might argue though that CAR T cells seem to be potentially getting rid of the tumors entirely and potentially even curing some patients altogether.

The problem is it doesn't work in everybody. And so, the question is how can we make it work better, make it more effective? How can we make it work in more people? And so usually that takes some combinations, but those combinations have to be developed carefully because the common theme of immunotherapies as a side effect is that they are activating the immune system. And so, while that's a good thing against the tumor, for the patient when you have an infection, and that's activating the

immune system in you, you have some side effects. You have a fever. You may have aches and pains and chills. You may have immune reactions that, in the case of CAR T –cells, can be life-threatening because those immune reactions can set off a storm of an immune response that can be quite uncomfortable and, in fact, quite dangerous in extreme cases.

And so, there's a balance of getting enough of that immune reaction while not too much of the immune reaction that the person can't tolerate it or has significant side effects. And so that's the double-edge sword. A lot of progress has been made in these immunotherapies to make them safer or to at least identify what the side effects could be and to monitor or prevent those side effects in a way that the tradeoffs are where we want them to be. But when you add an immune stimulant drug, for instance, to an immune therapy, you're going to get more side effects. And so that's why it's a stepwise process.

I do think that for many of these, they will be used in combination ultimately. But it's a very methodical and scientific process to make that happen.

Lizette: Sure. With all of these advancements, are we really looking at immunotherapies being utilized more for patients than more of the traditional therapies like chemotherapy, radiation, or even transplantation?

Dr. Leonard: I think that's a great point and a great question. This has been a rule of thumb in treating cancer and blood cancers, if you have a therapy that in some people can work when all the other standard therapies can't work – when chemotherapy is not working, when transplant doesn't work – but this new type of therapy in some people can work, then the obvious question is, well, why wait to use it as the last therapy? Why not use it as a first therapy or as a second therapy or as a third therapy?

And so, there are studies that are looking at that more and more. You then have to compare the effectiveness, and you have to compare the side effects of the treatment and decide is it something you save for later, is it something you do earlier?

So, for example, in CAR T cells, which are now approved for the treatment of certain patients with recurrent aggressive lymphomas, they were initially approved as a third line or a third treatment for people where the first and the second treatments didn't work. They were approved as a third treatment and could work there.

Now we have data from clinical trials that have compared CAR T cells as a second treatment versus chemo and an autologous, from yourself, stem cell transplant, which was the standard second treatment for people with these aggressive lymphomas. And showed that in patients who had a short remission to their first treatment, that CAR T cell is a better choice than chemo and an autologous stem cell transplant as a second treatment. So that's an example of it started as a third treatment, now it's approved for certain patients as a second treatment, and then the obvious question that some are exploring is, well, should we use it as a first treatment?

And I think the hurdle is going to be much higher. Do we have issues with more side effects and the side effect tradeoff? We have issues of the cost, of the practicalities, but I think we'll see more and more studies moving these newer therapies as part of the initial treatment or in earlier lines of treatment.

There's another example of this in Hodgkin lymphoma. The immune checkpoint inhibitors that we talked about, a drug called nivolumab and a drug called pembrolizumab. These are agents that were used as a third treatment, and now we're using them as part of the initial treatment or at least studying them as part of the initial treatment. And so again, I think that is really something that is a logical extension of the process, once you know something works later, moving it earlier can make a difference.

Lizette: Right, there has been so much advancement, even in the last couple of years. I think when we started out with CAR T-cell therapy, many of us were thinking that it was a bridge to having a transplant. Is it now something where it can be actually a cure for some patients, and that's why we're looking to see if we can do CAR T-cell therapy earlier?

Dr. Leonard: I think that's an excellent point. In CAR T cells, the initial curative therapy for most patients, is a chemotherapy-based approach. The second-line approach was chemotherapy and an autologous stem cell transplant for many patients; and that could cure patients, but a smaller subset. And then CAR T cells came on the scene, and in patients where those other therapies didn't work, this is again with aggressive lymphoma, largely diffuse large B-cell lymphoma, of that group of patients where the first and the second treatment didn't work, CAR T cells seem to give long remissions going out several years in about a third of patients.

So, I think that we do believe, generally, that in patients where the other therapies didn't work, CAR T cells can cure a meaningful number of patients. Now we don't have 20, 30, 40 years of follow-up, but we tend to think that in that type of lymphoma, perhaps in contrast to certain other types, but in that type, once you have patients getting out three, four, five years, that probably those patients or most of those patients are cured.

Now again, that's a third of the group falling into that population, which means that more or less there are two-thirds, where it either didn't work at all or it worked for a short period of time. So that's the group of patients we're trying a combination or trying a newer CAR T cell or trying something else or maybe using it earlier is where we hope that we can bump those numbers of patients to the point that we get more and more patients cured.

And so, yes, I think that once you see patients who've been through other treatments have long remissions, then it tells you that perhaps it's better than some of the earlier

treatments because they didn't work in some patients. So that's where we're trying to move things forward potentially in these combinations. And another scenario is acute lymphocytic leukemia, or ALL, where also in subsets of patients CAR T cells have been very valuable.

Lizette: Sure. I think it's really exciting. I know that you also mentioned bispecifics. And where are bispecifics right now? You mentioned that there's a process, right? So, are they still in trials? You did mention there's some bispecifics that have been approved. Where are we with bispecifics because I know that that's something that is newer to our audience.

Dr. Leonard: Bispecific antibodies, so the original bispecific or BiTE antibody treatment which is not quite an antibody. Its structure is a little bit different, so it's called the BiTE, a bispecific T cell engager. That is a drug, blinatumomab, which is also approved for acute lymphocytic leukemia, a subset of patients there. That's been around for several years.

But the bispecific antibodies that are bigger molecules, that are probably going to be used more extensively in the future, these are in clinical trials primarily in various forms of B-cell lymphoma and in multiple myeloma. We have bispecifics in clinical trials also.

These are really exciting. I would expect that we will have one or more of these available in the coming year. We have to see how that approval process goes.

The advantage of these, as opposed to the CAR T cells, which mostly need you to be in the hospital because of the side effect risk and the complexity of giving the therapy, not fully necessarily in the hospital, but by and large mostly in the hospital right now with CAR T cells.

The bispecific antibodies are more likely to be able to be given in the doctor's office and are more what we call "off the shelf". For our CAR T cell, if you decide today that

a CAR T-cell treatment is the right treatment for you, you have to set up the blood donation. You have to collect the T-cells through a fancy blood donation. You have to send it off to the company that's going to make the CAR T cells, and you have to wait several weeks, depending on the situation, to get them back. And so, you don't actually get the therapy for several weeks or even in some cases a month or two.

With the bispecific antibody, because it's the same drug that's given to every patient, it's more off the shelf. You can essentially decide to give it today and give it today or tomorrow. So that is something that is more convenient. It makes it a little more applicable because you don't have to figure out, well, we don't have to wait for several weeks. What are we going to do in the meantime if you're a patient who's sick? We can kind of get on with it pretty quickly.

And so that's an advantage as well as the fact that the side effect profile is a little bit easier for the patient to tolerate. On the flip side, we don't know that they work as well; and I think most people would argue that the efficacy is probably a little bit less, and we don't have years and years of follow-up to know how close they are to the CAR T cells in effectiveness, even if they're easier to tolerate and easier to administer.

Jesse: That is really great information, thank you! What makes a patient a good candidate for these treatments? Are there better options based on the type of blood cancer diagnosis, gene mutation, or other factors like age?

Dr. Leonard: It really is a very specific situation as of today where these forms of immunotherapy work. So, for instance, we talked about the immune checkpoint inhibitors as one example. Those work very well in Hodgkin lymphoma and in a type of lymphoma called mediastinal lymphoma, which is uncommon, but where they're also approved.

On the other hand, they don't work very well in follicular lymphoma. They don't work very well in multiple myeloma. So that particular category of drug would be good for certain types of blood cancer and not others.

CAR T cells are approved for certain types of blood cancer and not others. And so that's a different scenario, and in fact, it's not the same. They're not approved for Hodgkin lymphoma where the checkpoint inhibitors work. So, at the end of the day, it really comes down to what type of lymphoma or leukemia you're dealing with. That's one aspect.

The other aspect is you could have that diagnosis but depending on the therapies that you've had before the situation that you're in, or as you said, the genetic type where it matters more. So, for instance, in a type of lymphoma called mantle cell lymphoma, a small group of patients have a mutation in a gene called p53, in those tumor cells. That might be a patient where we choose CAR T cells maybe a little bit sooner than we would choose if you didn't have that mutation as an example.

So, it really gets into the nuances of the disease. It gets into where the drug's approved for because these types of therapies are only approved for certain scenarios. And the choices that a patient has are going to be very different based on what they've had before, what their diagnosis is, what their profile is. So, it's really something that a patient has to talk to one's doctor about very carefully.

But the good news is that these therapies are available to a much broader array of patients in general, than, for instance, allogeneic stem cell transplant, which used to be something that we couldn't do in older patients or frailer patients. And now the ability to get say CAR T cells is broader. There are patients who can't tolerate some of the aggressive stem cell transplants but might be a candidate for CAR T cells or could be a candidate for bispecific antibodies. So, it really does open this broad category of treatment to a larger number of patients.

Elissa: So, we have discussed with other doctors on the podcast about CAR T-cell therapy and why it works well with some cancers and not with others, and they talked about the targets that they're hitting that are on the cancer cells, but not on the healthy cells. Is that something that is the same with the other immunotherapies that

we're not able to find those specific targets on the cancer cell that would not be on the healthy cells, so it would be able to target that and leave everything else alone?

Dr. Leonard: That's a great point. Obviously, if the immune therapy has a specific target, and you don't have that target, it's not going to work. We wouldn't even try it in some cases. So, for instance, we use the CAR T cells that are approved targets, something called CD19. That is on B-cell lymphomas, so we use that CAR T cell in certain B-cell lymphomas that have that target. We don't use that CAR T cell in Hodgkin lymphoma, as an example, because Hodgkin lymphoma doesn't have that target.

Another layer of complexity is that one way that tumor cells can be resistant to CAR T cells is that they might lose the target. So, for instance, what we found in some patients with aggressive lymphoma is that they have that CD19 target on the tumor cell. They receive the CAR T treatment, and then in some patients who relapse, we find that the CD19 target isn't there anymore. The tumor cell adapted to essentially not have the target there, and that's a way that the cells became resistant to the immunotherapy. So, the target is a very important part of all of this, both in choosing what therapy for the patient is appropriate to try and also how that therapy may or may not work in an individual patient.

Elissa: Now you mentioned a little bit earlier, we were talking about side effects, how they're still having some side effects with these versus side effects with our traditional therapies. What are really the differences because we're not only talking side effects, but we also want to think about quality of life for these patients. And if we're looking at these new therapies, then I'm sure everybody can have concerns when new therapies come out if they're going to work, if they're going to feel really sick. What are really the differences between some side effects of these immunotherapies versus traditional therapies like chemo or radiation?

Dr. Leonard: It depends a bit on the specific treatment that we're talking about. For instance, the immune checkpoint inhibitors, because they're essentially unshielding the tumor cells from the immune system, they can have effects that the immune system is acting in an overactive fashion. So, it can cause inflammation of various forms.

So, for instance, inflammation of the lungs can happen. Inflammation of the thyroid gland can happen. Rashes can happen as part of an inflammation of the skin. So that's the broadest kind of way of thinking about these is it's an overactive immune system, and inflammation is part of the immune system being overactive and going after the normal tissues in one fashion or another.

Those are typically mild and manageable, and even if they happen for the vast majority of people, we now know what to do about that to treat it and to minimize those. But occasionally they can be pretty severe.

For the CAR T cells, the biggest thing is this cytokine release syndrome. This is something that, again, the immune system is active, so it's an overreaction of the immune system making these cytokines, these immune proteins that essentially are a super version of feeling like you have the flu where you get fever and myalgias or muscle pain or joint pain. And in its extreme forms, these immune proteins can cause inflammation of different sorts, including an inflammation of the brain. So the most serious side effect of the CAR T cells is a neurologic or a brain inflammation that can cause confusion or, in certain cases, even, almost kind of a delirium where the person neurologically has some issues.

Now this is almost always reversible and is quite manageable, and now that we know to watch for this, it usually is not an issue. But occasionally it can be serious, so that's something that is part of this process. It takes a specialized team to manage this, to look out for this, and patients, when then get these therapies, go through a very detailed discussion as to what can happen.

The other thing that's a bit more common is that the immune system can be suppressed for some period of time after this treatment because these CAR T cells, and the bispecific antibodies can knock out some of the normal immune cells. So, this is something, being worried about low blood counts and infections, is a much more common side effect of these things for more patients.

Now again, if you're a patient where you have very few other options, then this tradeoff is one that you'll put up with. But if you're a patient who has lots of other options, or it's early in their treatment and the standard treatments work pretty well, then you might say, "Hey, this isn't something I need or want to do right now because I have other alternatives." So, it really comes down like most things with the treatment, just sitting with your doctor, talking about your own individual situation, the risks, the benefits, and the options you have to decide is this something you do now? Is this something you're never going to do? Or is this something that you might do in the future, but for right now, you'll try something else and really understanding all of that.

Elissa: Right, and we're really adding on then a whole new complexity when we're talking about COVID and reduced immune system or getting the vaccine response with a different reduced immune system too, right?

Dr. Leonard: Exactly. And I think with COVID, we have to be careful with all of our therapies to make sure that we're not causing or having any other issues as part of it. And in the COVID epidemic, all of our therapies take on a new light as far as side effects. That does figure into the equation now. Again, most of the patients right now getting many of these therapies have limited other options; and their blood cancer is the main problem they're dealing with. We do have to be mindful of the infection risks and what we can do to minimize those challenges.

But again, for people who, where the current options maybe don't have the same immunosuppression side effects, we might kind of hold off on these more

immunosuppressive therapies to a later date if we have that choice. So, again, it comes down to the individual situation.

Jesse: For those listening who think they could be a potential candidate for these therapies, should they discuss with their doctor which options are available for their specific cancer diagnosis or ask about clinical trials? What would you say is the best approach?

Dr. Leonard: I think that anytime a patient is facing a new treatment for a blood cancer, even if that treatment sounds pretty good, meaning even the chance that that treatment will work very well and sounds pretty easy as far as side effects, there are always clinical trials out there that are exploring, is there a different way to do it? Is there a treatment that could work an even higher percentage of the time or a treatment that has even fewer side effects? So that, even if you're in a great situation and we're fortunate that a number of our patients are likely to have excellent outcomes with the standard therapies, there is still room for improvement. I think all of us would say in our treatments, with regard to trying to get to a point where we cure everybody, we're trying to get to a point where our treatments have even fewer side effects.

That being said, many patients, the options are limited. They are not as good as we would like. Maybe the chances are lower than we would like, or the side effects don't sound so good. And in fact, some people, unfortunately, the standard therapies are quite limited in what they can do; and so, there are scenarios where clinical trials offer something new.

And I would tell a patient who's thinking about therapy, or even if you're not getting therapy, I mean there are studies that are helping us learn about blood cancers , where we're just observing patients, not doing anything, not giving a specific treatment in addition, but just learning and gathering information or donating blood

samples as an example. All of these are scenarios where patients should pursue clinical trials or clinical studies.

These are often available in the local community centers, or in some cases you may need to explore options at larger academic centers. But many trials are available in the community. If you can't travel or don't want to travel, others again offer options that may be good options. And if you can go to another center, depending on where you're getting treated, that may give you other alternatives to think about.

So, I would encourage talking with your doctor. If your doctor doesn't participate in clinical trials, no doubt they can give you some advice as to where to look more into that. I know LLS has great resources to help patients learn about trials, whether it's just in general or to find a trial that fits for you or your loved one specifically, so LLS is a great resource for all of this as well.

Jesse: I'm sure our listeners greatly appreciate this information, so thank you.

Elissa: And you made a really good point about clinical trials as well and how patients can really get on them at any time if they qualify for a trial. LLS, of course, has our Clinical Trial Support Center where oncology nurses can look all around the country for patients to find a trial that they would qualify for. So, we really appreciate you bringing that up.

Now our final question for you, on our patient podcast home page, we have a quote that says, "After a diagnosis comes hope." With all of these new immunotherapies or those in clinical trials, what would you say to patients and their families to provide them hope after a diagnosis of blood cancer?

Dr. Leonard: I would say that after a diagnosis of blood cancer, really the future is quite bright; and the present is quite bright. I told a patient just yesterday that anything they read about their disease as to what the prognosis is or how people live

or how people do or what their chance of living whatever period down the line will be, that that is the past. And the present and the future are both very, very promising.

We have treatments now that we didn't have a year ago. A year from now, we'll have treatments that we don't have today. And we're getting smarter with every passing day. Clinical trials is really one way and research supported by LLS and other groups are really the way for the future to move things forward and to improve those outcomes. But really, there are patients listening today that over the course of their journey with their disease, they'll be getting treatments that we haven't even heard about or thought about, that we haven't even conceived yet because work that's ongoing will lead to a new advance months or years or decades from now.

We wanted that all to go quickly because the sooner we can bring these new advances to patients, it's really essential. It all comes down to time and money and participation in clinical trials, in clinical research so that we can really move things forward more quickly.

But there's a lot of reason for hope, I'm encouraged, and we haven't made as much progress for everyone as we'd like, but we're definitely moving in the right direction working together.

Elissa: Well, thank you so much, Dr. Leonard, for sharing all about immunotherapies. I think you're right. There is really so much reason to have hope for the patients that research is changing all the time and getting better. And just looking back at 2017, 2018 and how much we have grown in the amount of treatments available since then and the amount of clinical trials available is just truly amazing.

And so, we're really excited to hear all about these new and current immunotherapies and hopefully those will provide those better options for patients currently and then in the future. So again, we really appreciate your time today.

Dr. Leonard: Thanks very much for having me. It's been a great discussion.

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.

To help us continue to provide the engaging content for all people affected by cancer, we would like to ask you to complete a brief survey that could 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.

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

Have you or a loved one been affected by a blood cancer? LLS has many resources available to you – financial support, peer-to-peer connection, nutritional support, and more. We encourage patients and caregivers to contact our Information Specialists at 1-800-955-4572 or go to LLS.org/PatientSupport. You can also find more information on immunotherapies at LLS.org/Immunotherapy. Clinical trial support can be found at LLS.org/CTSC. All of these links 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.