LEUKEMIA & LYMPHOMA SOCIETY®

THE BLOODLINE WITH LLS

A PODCAST FOR PATIENTS AND CAREGIVERS

Episode: 'CAR T-cell Therapy Explained: What is it and How Does it Work?

Description:

Join Alicia and Lizette as they speak with Dr. Rayne H. Rouce. Dr. Rouce is a pediatric hematologist and oncologist at Texas Children's Cancer Center where she is a member of the Leukemia and Bone Marrow Transplant programs. Specifically, she works as part of a research program called The Center for Cell and Gene Therapy at Baylor College of Medicine, focused on translating targeted T-cell therapies from the bench to bedside, and has been involved in every aspect of CAR T-cell development for clinical use. On this episode, Dr. Rouce explains the process of chimeric antigen receptor T-cell therapy, also known as CAR T-cell therapy. She also explains the role of normal T cells, how re-engineered T cells are expected to perform after being reinfused into the patient, and the lifespan of these re-engineered T cells. Dr. Rouce shares her excitement not only for the future of CAR T-cell Therapy but also for the hope that this therapy provides to many patients and caregivers.

Transcript:

Alicia: Welcome to The Bloodline with LLS. I am Alicia.

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

Alicia: Today, we will be speaking with Dr. Rayne H. Rouce. Dr. Rouce is a pediatric hematologist and oncologist at Texas Children's Cancer Center where she is a member of the Leukemia and Bone Marrow Transplant programs. Dr. Rouce has spent the past several years of her career pioneering immunotherapy research for patients with refractory leukemia and lymphoma. Specifically, she works as part of a research program called The Center for Cell and Gene Therapy at Baylor College of Medicine, focused on translating targeted T-cell therapies from the bench to bedside, and has been involved in every aspect of CAR T-cell development for clinical use. She has significant clinical experience in taking care of patients who have received CAR T-cells and is passionate about ensuring patients and families understand this exciting new therapy. Thanks so much for chatting with us today, Dr. Rouce.

Dr. Rouse: Hi. Thank you so much for inviting me. I'm really excited.

Alicia: Good; yes, so are we. Now, for our listeners, Dr. Rouce is no stranger to The Leukemia and Lymphoma Society because we actually did a program with her and Dr. Loretta Nastoupil from the University of Texas MD Anderson Cancer Center in Houston, Texas in which they spoke about CAR T-cell therapy in children and adults blood cancers. So, for those listening, we encourage you to visit www.lls.org/programs to view that program. So, thanks again for joining us.

Dr. Rouse: Of course.

Alicia: So, before we get into the meat of this episode, we are always interested in hearing about how speakers got introduced to their field. So, for you, what brought you to the field of medicine? Was it something that you knew you always wanted to do?

Dr. Rouse: Well, I think the story may be pretty similar to a lot of physicians. I knew that I wanted to do something. I was taking care of people. One of my greatest fields of talking—and some would say I may talk a little bit too much and put them to the test.

Alicia: Same.

Dr. Rouce: I love to hear about people problems. I love to try to help them. So, I initially thought I would be a psychiatrist, and then once I got to medical school and I did my very first pediatric rotation, I absolutely realized that I needed to take care of children. So, I decided to do pediatric. I never actually thought I would end up taking care of kids with cancer, but from the first time that I ever took care of them, I knew that it was kind of my calling.

You guys know that we have to treat patients with leukemia, for example, for a really long time; and so, you really get to become a part of their family. You watch them grow up. I have patients that I have taken care of since they were 2-years-old, who are now teenagers and pretend like they don't know me. So, I love that aspect of it and I would never trade it for anything.

Alicia: Right. We were actually speaking with another doctor who said he feels like he's part of the family in helping them make very important decisions at such a challenging part of their life.

Dr. Rouce: Absolutely. So, it truly, in some ways, I practice psychology and psychiatry every day. Not just with the patients and the families, but with everyone, you know, working as part of a team. So, it's really kind of the best of both worlds.

Alicia: Right. So, on today's episode, we are going to be talking about CAR T-cell therapy.

Dr. Rouce: Yes.

Alicia: And, it's interesting because over the past several years, you hear immunotherapy. you hear that it has emerged as—I was reading an article where they referred to it as "the fifth pillar of cancer treatment" so…

Dr. Rouce: Absolutely.

Alicia: Yeah; what is this for the listeners, for patients, the caregivers listening because it seems like something that people are asking everyone about? They are certainly calling up and asking us about. So, what is this for those listening?

Dr. Rouce: Absolutely. And also mention, you know, 10 years ago, it was difficult to find someone who actually knew what CAR T-cell therapy is and now, you know, we have our grandparents calling us saying, "have you heard about this therapy" because it is so widespread and so well known.

So, I am going to break this down and simplify it. So, a lot of times when people talk about immunotherapy, they use it almost synonymously with CAR T-cells because it is one of the, I think, most well-known types of immune therapy and, basically, what this means: a CAR T-cell stands for Chimeric Antigen Receptor T-cell. That's a mouthful! Any time you hear CAR or Chimeric Antigen Receptor, all that means is that this is an artificial receptor, okay, that we've engineered in the laboratory for the sole purpose of specifically recognizing something we want it to, okay? So, when we make CAR T-cells to target cancer, we take T-cells, typically from a patient with cancer. We trick them into the laboratory where, basically, we put them inside of cell culture plates and we use a virus that's inactivated to introduce into it this special machinery that will cause every T-cell in the culture to express, on its surface, this artificial receptor. Again, the purpose of that receptor is to target only what we want it to. So, you can essentially make a CAR T-cell to target almost any antigen or marker or surface protein that's on the surface of someone's cancer. So, once we introduce this new machinery into the T-cell, and a lot of people—I mention this genetic engineering because these are what we call genetically modified T-cells, meaning we are putting something into its DNA, into its make-up, to make the T-cells different. We feed them, and grow them in a laboratory, and expand them until we have enough that we can give back to a patient. So, it's a personalized therapy, but it certainly is one that has taken a lot of technology to get there.

Lizette: And there are T-cells right now in our bodies, aren't they there to attack when we're sick?

Dr. Rouce: Absolutely. So, T-cells—all of us have T-cells that are floating around our body and their job is to be on surveillance. I like to call them the security guards. So, they are floating around the body and they have a regular T-cell receptor on them. We call it a native T-cell receptor. It was born there. It has been there. And that T-cells receptor's job is to look for things that don't belong. So, that could be a virus; that could be some sort of bacteria, but importantly, it could also be a cancer-infected cell, okay? So, most of us make a few bad cells every day that don't look quite right and our T-cells will go after them, attack them and use their killing machinery to kill them. The problem is very few of us, even patients with cancer, have T-cells that are specifically made to actually recognize something that's on a cancer cell. So, they may recognize that the cancer cell is not quite right in some way and doesn't belong there, but it's not specifically geared to target. So, when we take T-cells from the patient's body, we don't remove those regular T-cell receptors that exist, we just add our special artificial CAR receptor so that it can equip the cell with another kind of enhanced healing ability, specifically against something that's on the cell of the—on the surface of the cancer cell, rather.

Lizette: So, that's how they know to actually attack the cancer cells since they haven't been attacking the cancer cells before.

Dr. Rouce: So, another thing about T-cells is when they have been in contact with things—so they may attack a cancer cell here or there, but if you have a lot of cancer cells in the body, they get overwhelmed. They can get a little bit lazy. They fall down on the job. So, what we do is we take these T-cells out of patient's body. We wake them up in the laboratory. We stimulate them by feeding them with nutrients that make them kind of get souped-up; and then we train them to attack what we want them to. So, not only do we expand them in number, but we really kind of simplify what they look at so they don't get distracted. Sometimes, T-cells in your body are like, "oh, here's a virus over here. Oh, here's this over here."

We taught these T-cells to go in and keep their eye on the prize, which is the cancer cell, identify it, because it has a special receptor that's built to identify those surface markers, target it for killing, and then use it's killing machinery to kill it and eliminate it. The good thing about CAR T-cells is that they get really excited once they come into contact with cancer cells. They kill them, and they get excited, and they recruit their buddies over and they say, "hey, let's kill some more," and they grow in number and they kind of get activated, you'll hear us say, and they just "go to town" against cancer cells.

Lizette: Wow

Alicia: I think it is so fascinating when we were first introduced to this process, I know, you know, we did videos—on it; we did publications on It, and I remember just reading it and saying "what is this?" trying to actually grasp It; and I think your explanation that you just gave is one of the clearest explanations about CAR T-cell therapy that we have heard.

Dr. Rouce: It really is futuristic-type medicine, and it's hard to wrap your head around, but the interesting thing is that it—it capitalizes on the basic immunology of the body. T-cells are supposed to look for viruses. So, we trick the T-cells and we use an inactivated virus to put it into the T-cell carrying the machinery that actually is the CAR. So, we kind of use the T-cells on tricks against them to get the CAR molecules to attach to them; and then we grow them in number and we put them right back into the patient; and then they go and kill the cancer.

Lizette: Well, I think the coolest thing is that it's your own cells.

Dr. Rouce: Absolutely.

Lizette: You know, it's not like getting chemotherapy, which is a combination of medications, to come into your body to kill cells. It's actually your own cells that are recognizing these cancer cells and doing away with them which is exactly what you want your body to do.

Dr. Rouce: Exactly. I think that is one of the greatest things about CAR T-cell therapy is that it truly kind of empowers the patient. You know, most patients who ultimately will receive CAR T-cell therapy, are patients who received other forms of therapy in the past. You mentioned chemotherapy; sometimes radiation; sometimes a surgery; sometimes other experimental drugs. This therapy allows your body to kind of take control and none of our bodies will be able to do it on their own so we have to use our special laboratory medicine to soup-up the T-cells, laying them out, like I like to tell our teenage patients…

Alicia: I love that.

Dr. Rouse: ...laying them out in the laboratory.

Alicia: So, when hear, re-engineered T-cells, I, you know, again, when I first heard about this, I said, "okay, that's fine". How long do we expect these re-engineered T-cells to work, but it's indefinitely, right?

Dr. Rouse: That's an excellent question. So, one of the ways that we have made the greatest strides in CAR T-cell therapy over the last few years is in making these T-cells

last longer. So, on one hand, they are your own cells, right? So, you don't have to worry too much about your body recognizing them as foreign because they have the same HLA, or tissue-type, that's used. You don't have to worry about that, but on one hand—the original version of CAR T-cells was not designed to last forever because it relies on the T-cells own kind of killing machines. What we have since learned is that there are a couple of things that we can do to make them last longer.

One is just like we build the CAR receptor into the T-cells. We can actually put additional stimulatory molecules that their only job is to make the CAR T-cells last longer in the body. So, these help the CAR T-cells persist, okay?

The second thing we realize is if we make room for the CAR T-cells, like giving a few days of what we call "lymphodepleting chemotherapy", which is kind of like chemolyting; so a few days of chemo, then we clear out some of the other lazy T-cells that weren't really doing their job anyway, and we make room for our CAR T-cells to come in and set up shop. So, there are lots of differences. Every CAR T-cell is created differently, okay? So, one of the biggest advances, I think that truly have made in the immunotherapy world is knowing that unless a CAR T-cell has additional built-in stimulation, it's very unlikely that it is going to last in the body for as long as we want it to. The reason that it is important for the CAR T-cells to last for a long time is because if we can't find the CAR T-cells in the patient's blood, we always worry that the cancer will try to come back because it doesn't have that CAR T-cell hanging out in the blood, in the bone marrow on surveillance looking for it. Does that make sense?

Alicia & Lizette: It does.

Alicia: So, you mentioned that, every CAR T-cell is created differently. I know that, at different institutions, the process kind of differs slightly as well. So, does that even make the situation hairier when it comes to approaching how a team might think the CAR T may perform in the person's body and for how long?

Dr. Rouce: Absolutely. That's a great question. So, in the earlier days of CAR T-cell therapy, we did not—and when I say earlier days, I mean even as early as, like, 10 years ago, okay?

We really didn't know which properties were most important for CAR T-cells, okay? And once we identified, even in the laboratory and in free clinical studies with mice, we realized that the T-cell's ability to heal alone, even with the CAR molecule attached, was good, but eventually those T-cells will get tired, and they get lazy, and turn off. So, we knew that we needed to add something additional to the CAR to make it keep going and keep killing. We did not know what the ideal additional molecule was. So, interestingly, and this is—this is where it gets really confusing for patients and for caregivers, also, because you say, "okay, I see these 3 different CAR T-cell studies.

They all say they are targeting the exact same molecule, let's say CD-19 on B-cell malignancies and they look the same, but they're 3 different completely studies. How are they different?" Often, the main difference is that the additional stimulation molecule that researchers added to the CAR was different, okay? Initially, this was because we had to study these in early phase trials, some of which the LLS supports, and we had to figure out which one was best. Now, there are a couple of commercially available CAR T-cells. One of them uses one of the main co-stimulatory molecules, and the other uses the other. The reason why is because the result has been similar, meaning we can induce complete remissions in lots of relapsed patients with these CAR T-cells, but it is clear that one of the additional molecules does things to make the cells last the longest, okay?

I would say now we are finally at a place where we have been able to explore the properties of these CAR T-cells more in patients in clinical trials and, even on a commercial setting, so we kind of know what you get based on the different CAR T-cells; if that makes sense. So, there might be a reason that a doctor says, "you know what, I am going to choose this CAR T-cell for my patient because I'm trying to get them to a sibling match transplant because this is still what we know provides a long-term period option. And although we do have lots of patients who are 5-6 years out from CAR T-cells, and going strong, and have had no other therapy, it is still a relatively new therapy so we don't really know, on a large scale, how long they last." Whereas, if someone did not have a transplant option, you might say, "you know what, this CAR T-cell has this additional stimulation molecule that, in clinical trials, has been shown to last the longest. So, I am going to choose this option because I hope it will be an ultimate curative option for my patient." Does that make sense?

Lizette: That does make sense. I was going to ask you, because, in the beginning, when we started hearing about CAR T, we didn't know if CAR T was for a cure or just as, like, a bridge…

Dr. Rouce: Exactly.

Lizette: … to another therapy.

Dr. Rouce: And that's a great question to bring up because, initially, everyone thought of it as a bridge. The reason that we found out that maybe this actually is for a cure is because some patients, who either were ineligible for bone marrow transplant, or did not have a donor, or decided to wait and see, actually remain in remission long-term. And we find these CAR T-cells still circulating in their body years out from therapy. So, it still remains unclear who will have a long-term remission and who won't, but the good news is that we have very good surrogates for measuring. So, we can easily track these cells in the blood. So, if you have no evidence of your

cancer and those cells are still happily floating around, even if in a very low level, most of us feel really good about it and we say, "you know what, you are still going strong." I think we are still several years away from truly being able to say whether CAR T-cells can be curative for some patients and what distinguishes a CAR T-cell that is potentially curative versus one that is more of a bridge. And I think our definition of bridge will change. You know, originally, a bridge is 6 weeks, 8 weeks, 3 months or so to the next therapy but, we may find that a bridge may be longer. It may be 3 years, 4 years, 5 years and that's still a really long time especially in patients who previously were told that they didn't have treatment options.

Alicia & Lizette: Right. Right.

Alicia: I can only imagine the excitement for patients and caregivers. I know that, within the healthcare field, it is one, like you said, it's one that, , is expanding and transforming based off what new information comes about, but for patients and caregivers, who were told, or would have been told in the past, that there's nothing for them, this is such an incredible option for them. So, I thank you for all that you do for these patients and caregivers.

Dr. Rouce: Of course. I mean, I am honored to be a part of CAR T-cell therapy research and to work with a team that is able to support these efforts. It is a huge on-taking, not just for the patient, but for their families, and their caregivers, and other healthcare providers who send patients to us and organizations, like yours, that support this research. So, it's really amazing and I think every day, at least twice a day, I think about patients that I took care of early on in my Fellowship when this was not a treatment option and I think about how things may have been different had it been. And I think that that's—it's probably what every physician who has ever, or healthcare provider, who's ever taken care of someone who successfully got in CAR T-cell therapy, or not successfully gotten it, thinks about. And it is also another reason why none of us are content to just stop now. We are always looking at ways to make CAR T-cells better. It is like going from the Model T to the Tesla, right? You know, there's always something.

Alicia: That's right. That's a great example.

Dr. Rouce: There's always going to be upgrades. We're trying to get to the line CAR features setting, right?

Alicia: Yes; yes. people call the LLS and they say, "I heard about this new option. Tell us more about it." Or, we will talk to doctors who will say, "we have a, you know—we have a flood of people coming in and asking about this new therapy." So, when someone comes into your office, are there any common questions that you find that are being asked by patients and caregivers?

Dr. Rouce: Absolutely. I think one thing that we always have to remember, and this is a big take-home point, is still, at present, even though CAR T-cells are commercially available for some malignancies, such as leukemia and lymphoma that express CD-19, the one thing to remember is that these CAR T-cells are still reserved for use in patients who relapse, meaning have their cancer come back or who have been unable to go into remission. This is still not front-line therapy. This is why when patients may go to their doctor and they are newly diagnosed with a type of cancer, they say, "you know, I heard about this potentially less toxic, more personalized option, I'd like to do this. I'd like to be eligible for CAR T-cells"; and their doctor has to say, "unfortunately, right now, or fortunately, you're not eligible because this is only available for relapse." And the reason why is we still do not have enough long-term data on CAR T-cells for it to move to the forefront of therapy. I don't want people to be discouraged by that because, what this also means, is we are in a different realm now. Now, if you, unfortunately, have your cancer come back, you have more options that you previously did not have to treat. And these are actually pretty good options. You know, not options that say, "well, there's a 10% chance, or a 20% chance", but with CD-19 CAR T-cells, for example, there's upwards of 70% chance that lots of patients will experience a complete remission after them, which is really great.

Also, I don't want people to be discouraged because every single day researchers who deal with CAR T-cells are working on how can be move this therapy to the forefront, okay? How can we move it earlier in treatment? How can we give these cells before people actually relapse? How can we use it up front and maybe stop using some of the more toxic mechanisms? In order to do that, we have to study it very faithfully, right? We have to build it into clinical trials. We have to first say we are only going to reserve this therapy for people who show evidence early on that they may not continue to respond to our traditional mechanisms of treatment. So, there still is a waiting period before this comes to the forefront, but I think it is a necessary waiting period because we need to know everything that we can know about CAR T-cells and who is the ideal person to get them before we actually give them—give them to patients.

So, one big question is, am I eligible? People always ask that and, often people who don't quite meet the criteria because they are still receiving initial treatment or they have no evidence of the disease, they haven't relapsed will feel a little bit downtrodden by this, but I encourage them that, you know what, we have this in our back pocket if you ultimately need it, which we hope you never do.

The second thing is that in order to be eligible to receive CAR T-cells, your tumor has to actually express what the CAR T-cell is targeting, okay? So, this is not so big of an issue for CD-19-positive B-cell leukemias and lymphomas because the vast majority of them express CD-19, but this does become an issue for some of our other types of even acute lymphoblastic leukemia, such as T-cell ALL. It becomes an issue for AML.

It becomes an issue for multiple myeloma, which adults get. It becomes an issue for almost any other cancer that you are targeting. It can be difficult to find a surface marker that is present in uniform expression levels on the vast majority of people's cancers. The reason that it is important for that marker to be present is that, if you target a subset of those cancer cells; let's say you knock out 50% of them, you still have 50% there. Then, they are going to be much angrier and ready to come back. So, we have to be very safe when we are choosing who we give this therapy to.

Lizette: You know what you're saying, Doctor, we hear people who want to go into CAR T all the time as their initial therapy and we've actually—Alicia and I have spoken to a gentleman who's gone through CAR T therapy and it was for, you know, a subsequent relapse and—and how nice it would be that maybe, at first relapse, he was able to get this. So we do hear the frustrations from people all the time that, you know, everybody is looking for something that's not as toxic, because we keep hearing that, you know, chemotherapy, radiation—this is all, very harsh on your body. Now, is CAR T also very harsh on your body?

Dr. Rouce: Very good question. So, we talked about how the T-cells are personalized. They're made from your body. We engineer them in the laboratory. I haven't mentioned yet, but we obviously test them extensively to make sure that they target what we want them to and they don't target what we don't want them to. So, they're very well-tested and dutifully tested before we put them back into the body. One thing about CAR T-cells, though, is that when they come into contact with a tumor, they are primed to heal. They get super excited. They get really activated. I told you they call other buddies. They are like, "hey, what is going on here…? …everyone in the neighborhood. Even the people who are normally sleeping and being lazy, they recruit them. So, they really activate the immune system, but what can happen is when all these T-cells, kind of, attack cancer cells, your body can release a lot of different inflammation markers; and the reason why this is important—these are called cytokines—but these cytokines can cause you to have fever. They can cause you to feel like you have the flu. They can even cause you to look, to any healthcare provider, like you have a bacterial infection. So, the CAR T-cells when they are attacking cancer cells, can make you pretty sick. Sometimes, this can require you to be transferred to the Intensive Care Unit. You can need help with keeping your blood pressure up using medications. You can need additional support to help you breathe. This is called cytokine release syndrome and is actually very common with the most common CAR T-cell, the CD-19 CAR T-cell. So, lots of care has to be taken into treating patients. We know that this can occur. We know the main inflammatory (inaudible) that causes it and we actually have an antidote to it. So, we know that after people get infused with CAR T-cells, we have to watch them very closely. Most clinical studies, and even the commercial products, require patients to stay within about an hour or two from the hospital within the first month. Some trials require you to stay in the hospital. The reason why is because we can't exactly predict when these

symptoms might occur, but usually it occurs when the T-cells get really activated and start expanding; and I would say, on average across most studies, it is about a week, okay? But it can occur as early as 24 hours. And so, even though this can happen and we have a medication, and other medications we can give to kind of dampen these symptoms, so we can treat it. It is usually transient and is something that typically goes away. It can certainly make you very sick, okay? These cells also can find their way to the central nervous system. They can go into the spinal fluid. This can be a good thing because leukemia and lymphoma especially likes to find its way there, too. So, they can go there and be on surveillance, but they can also, sometimes, cause you to have some neurologic symptoms. It could be something like sleepiness, but it can also be seizures. So, there's a lot of precautions that we have to take. The good news is these side effects are typically transient and we have very detailed diagnosis and treatment algorithms that are widely available, but this is part of the explanation for why, if you live in a very small town and you have an amazing oncologist that you love that you go to there, they may say, you know, "unfortunately, we don't have CAR T-cell therapy here" because it requires quite a big infrastructure to be able to safely take care of patients.

Lizette: So, a type of infrastructure, like transplantation?

Dr. Rouce: So, good question. So, the type of infrastructure, meaning #1, to make the cells—there are places that make the cells there, in-house; like, for example, in our Center for Cell and Gene Therapy, we make lots of different types of T-cells and you do need what is similar to a transplant structure there, but you need a special laboratory to make cells. Or, I think the CAR T-cells that people are most familiar with are where they have their T-cells collected you know, at pheresis centers, and some smaller hospitals don't have pheresis capabilities, and they may refer patients to other pheresis centers. And then your cells are sent to a company, for example, or a factory to make the cells. So, in order to treat patients with CAR T-cells, you have to have an ICU. You have to have the Emergency Department. You have to have doctors who are certified to take care of patients who had adverse events from cell therapies, which typically means you have to have a bone marrow transplant program. So, that sort of infrastructure.

So, also because these symptoms can happen as early as 4 hours after the cells, or they can happen 2 weeks after the cells, it's really important that you be able to stay within a certain distance to that hospital because we would hate to send a patient back to their home oncologist, who may be an amazing oncologist, but the hospital doesn't necessarily have the infrastructure to take care of a patient who has a specific side effect from CAR T-cells. And you can imagine that if you are at a large Center, like ours, we take care of lots of patients who receive CAR T-cells so our Emergency Room doctors, our ICU doctors, all have to be trained as well to identify immediately, and not just the doctors, but the nurses, and the coordinators. So, it's quite a big undertaking

and I think that, you know, one of our biggest goals is to make the therapy more widespread and to make it more available. So, I think that that's something that we are all working on, as well.

Alicia: And I think that for our patients and caregivers listening, they hear CAR T, they get excited about it. They want to know more about it, it's a process and it does take, like you said, it takes a team. It takes, you know, a qualified team to make sure that they are giving the best care and they feel like they are receiving the best care as well.

Dr. Rouce: Absolutely; and I think, luckily, especially with the help of people knowing about CAR T cells and patients asking about CAR T cells, caregivers and organizations like yours, even if your home institution doesn't have the ability to collect your cells to make CAR T cells or send it to a company, etc., they usually can identify a place, at least in your region now. And this was not the case, you know, just 5-6 years ago. You may have to travel across the country.

Alicia: Right. And just going back to what you said earlier, we know that CAR T therapy is FDA-approved as a standard of care for some forms of cancer, but, you know, there are clinical trials out there that are improving people's quality of life and here, at LLS, we have a service called the Clinical Trial Support Center and, what it is, is that patients can work one-on-one with an LLS clinical trial nurse navigator who will, assist them throughout the entire clinical trial process. So, I think it is very important for services like that to exist and, for those listening, you can call 1-800-955-4572 or visit www.lls.org/informationspecialists and complete the referral form. and that way, they can ask the question about clinical trials, see what's out there because it can be overwhelming.

Dr. Rouce: I am so glad that you mentioned that because even for me, as a physician-scientist who does CAR T-cell therapy, when I go to clinical trials just to see what new trials are out there, I get overwhelmed. My colleagues, who are leukemia and lymphoma specialists, get overwhelmed. So, I think it is amazing that LLS has this. I have been contacted a number of times; and a number of times by LLS patient advocates who are looking for trials and have found—identified a trial of mine that may be suitable for one of the patients that has contacted them. And even if they are not necessarily eligible, they link them with me and I can link them with colleagues across the country, and sometimes the world. You can say, "you know what, here's a potential option." And this is something that's very difficult for anyone to navigate on their own whether you are family, a caregiver or even a healthcare provider.

Alicia: Absolutely. And when I went to that website clinicaltrials.gov, amazing list of clinical trials, but for somebody who may already not be feeling well or for a family

member who has no idea of what this new world is about, it can be so overwhelming. So, I think this…

Dr. Rouce: It is overwhelming.

Lizette: Yeah.

Alicia: …is perfect.

Dr. Rouce: I'll tell you a secret. If I want a …

Alicia: Ohh! We love secrets. Tell us.

Dr. Rouce: I'll tell a secret that's going to be on a podcast, right? What colleagues, who we may have some friendly competition or doing, I often look at the LLS website because you guys keep us really up-to-date and I often reach out to you guys first because, as you said, the clinical trials website is amazing, but it can be a little bit difficult to navigate.

Alicia: Absolutely. Patients and caregivers listening, share that secret because it is one that can literally improve your life.

Lizette: Yeah; and it's important to take everything into consideration and our nurse navigators do. So, if you don't live in a place, like Dr. Rouce said, that they have CAR T-cell therapy we'll look to see where they do have CAR T-cell; and to see if it is feasible for you to travel, because there's so many things that go into traveling—caregiver issues; there's financial issues. All these issues that we want to take into consideration when looking for a trial for you. So, that list of 200 possible trials could go into, you know, a good 10 that may be really applicable for you, not just because of a certain mutation you have the diagnosis you have, but also what is going on around you and what your needs are.

Dr. Rouce: Absolutely.

Alicia: Before we end this episode, Dr. Rouce, is there anything you want to share with our listeners that we haven't mentioned or you think is a point that needs to be stressed?

Dr. Rouce: I think I'd like to say that I often, when I do programs like this or even when I'm talking to friends or family members who may know someone who has been diagnosed with cancer, and they have a cancer that, right now, there aren't a lot of clinical trials using CAR T-cells or there weren't maybe, perhaps, not any clinical trials, I want to let everyone know to continue to have hope. There are lots of researchers who have dedicated their lives to try to bring CAR T-cells to other types of cancer

therapy and not just cancer therapy. So, just because something is not available right now does not mean it won't be in 6 months or a year, or 2 years. So, continue to have hope. Continue to stay informed. Utilize organizations like LLS to your benefit and we are working hard to try to get there.

Alicia: Thank you so much for that, Dr. Rouce, and for joining us today and sharing such great information about CAR T-cell therapy with us. I know that our listeners and caregivers will learn just as much as we did about this incredible treatment option. So, thank you so much for your time.

Dr. Rouce: Absolutely. Anytime guys.