LEUKEMIA & LYMPHOMA SOCIETY®

THE BLOODLINE WITH LLS

A PODCAST FOR PATIENTS AND CAREGIVERS

Episode: 'CAR T-cell Therapy Explained: Understanding Potential Side Effects'

Description:

Like any therapy that is administered in oncology, there is great promise but also, unfortunately, several toxicities and side effects that must be understood and monitored. Join Alicia and Lizette as they speak with Dr. Jonathon B. Cohen, an Assistant Professor in the Department of Hematology and Medical Oncology at Emory University School of Medicine in Atlanta, Georgia. On this episode, Dr. Cohen explains the potential side effects of chimeric antigen receptor T-cell therapy, also known as CAR T-cell therapy. He describes how side effects may change over time and how a patient's family members and caregivers can identify some of the more subtle neurologic toxicities that can potentially lead to more severe side effects. Dr. Cohen also shares great information about what patients can ask their doctors about CAR T-cell therapy and things to consider when having this conversation.

Transcript:

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

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

Alicia: Today we will be speaking with Dr. Jonathon B. Cohen. Dr. Cohen is an Assistant Professor in Hematology and Medical Oncology at the Emory University School of Medicine. Dr. Cohen's research focus includes the clinical investigation of lymphoma where he aims to identify prognostic markers and designs clinical trials of novel agents for patients with relapsed disease Dr. Cohen is the clinical lead for implementation of CAR T therapy in lymphoma at Emory and also directs clinical trials involving cellular therapy in lymphoma patients.

Thank you so much for joining us today, Dr. Cohen.

Dr. Jonathon B. Cohen: Thank you so much. I'm glad to be here with both of you.

Alicia: Dr. Cohen, we're always interested in hearing what brought doctors to their field. What brought you to the field of medicine, specifically oncology?

Dr. Cohen: I was always very interested in science as a child, but I have to be honest, I never have one moment where I knew that medicine was exactly what I, what I wanted to do. I enjoyed learning about biology; and when I got to college, I started down the premed track and, honestly, became more excited. I find that a lot of people have the opposite experience where they are interested in medicine, and they start some of the pre-medicine requirements and find that it may not be for them or they may want to go down a different path, but I really enjoyed my chemistry and my organic chemistry classes.

And by the time I got to medical school, I had met my wife. We were dating at the time; and her father is an oncologist, and both of us have had family members who have had cancer. And I had the opportunity to really get to know him and go to work with him at times; and I was really drawn to the field of oncology from an early, early time in my medical career. I really enjoy the fact that you get to know patients and their families quite well, that you really get to know them over a long period of time. And even in the unfortunate situations where patients may not have the outcome that you would like, it's a really, great experience to be able to work with families through challenging times and really get to see them come together and help them manage whatever symptoms or other issues that a patient may be dealing with. And so, I find it to be an incredibly satisfying career.

Alicia: That's wonderful. It, it's always so interesting hearing. We had one doctor who said that he wanted to be an astronaut. We had another lady who was a director of an art gallery. So, we love hearing, what piques the interest of people and why they choose their field and do the great work that they do. So thank you for, for all that you're doing for your patients.

Dr. Cohen: Oh absolutely. No, I enjoy it. My wife and I joke that if I hadn't done this, I'd probably would have ended up doing something like meteorology. I've always been fascinated by the weather. But the truth is, it didn't take me long to realize that this is really where I wanted to be, and I couldn't see myself doing anything else.

Alicia: Right, we always hear also that those doctors who chose oncology, they always say that they love being a part of somebody's life at such an intimate time, when they're diagnosed with a cancer.

Dr. Cohen: Absolutely. And it, it's a really interesting experience, for me and can be very, very satisfying and challenging. You, we meet people early on, often right after their diagnosis and, and work with them and their family to help them understand their diagnosis and the prognosis and treatment options. And then you often have a chance to really work with them throughout the entire spectrum of their disease course. Fortunately, many of our patients respond very well to therapy; and you get to see them move on and have children and, and build their families or get back to work and, and resume their life. And that's always incredibly satisfying.

Some of my favorite visits with patients are those that are two or three years out, and we talk about exciting trips that they've had; and usually they, they're doing things that are a lot more exciting than I am, and it's just good to hear about what they're doing with work or, or travel or with their families or get to see them have, you know, get to know their grandchildren and so forth.

Lizette: Yeah.

Dr. Cohen: So it's, very satisfying, and, it's an area where you really can make a big difference in the lives of patients.

Alicia: Absolutely, that's wonderful. So, in today's episode, we're going to be speaking about CAR T, and there's so much buzz about or around chimeric antigen receptor T-cell therapy, also known as CAR T-cell therapy or CART. And we know that surgery, chemotherapy, and radiation therapy have been the foundation of cancer treatment; but due to exciting advances in the field of immunology, it has led to a greater understanding of the ways in which the body's own defense can be used for treatment of blood cancers.

So for those listening who may or may not be familiar with CAR T, what is it, and why are scientists excited about this option for treatment?

Dr. Cohen: CAR T is one of a number of new therapies that are either underdevelopment or now, fortunately, FDA approved that attack cancer in a new way. And so we've known for a long time that one of the ways that cancer grows in the body, especially hematologic malignancies like lymphoma, is that it evades the immune system.

And so normally when you're exposed to an antigen, whether that would be, a virus or bacteria or a cancer or something that's foreign to the body, the hope is, is that the immune system learns to fight off whatever that is; and then you get better. But,

unfortunately, cancer cells often produce chemicals that evade the immune system or shut it down; and this is what allows them to grow.

And so there's a new area of research in, in lymphoma and in a number of other, malignancies where we are learning to reactivate the immune system and use the body's immune system to actually fight the cancer.

And so what CAR T-cells do is that they actually are T-cells that are administered to the patient that target the specific cancer. And so we have T-cells in our body that target any number of different foreign agents, foreign antigens. And what happens with CAR T-cells is that they are engineered in a fashion that they recognize one of the signatures of the cancer. So for non-Hodgkin lymphoma, the one that's currently FDA approved is an agent that targets CD19, which is a known marker of B-cells, in B-cell lymphomas and in acute lymphoblastic leukemia.

And so these are T-cells that identify cancer cells that express CD19 and take them out. It's a really exciting new area of research, and we've really had remarkable results.

And in the past, for some of these patients, we've had very limited options or the options we've had have been highly toxic chemotherapy approaches. And so to be able to offer this to many patients has been a really exciting thing for us.

Lizette: I think it's really exciting to hear something that involves our own immune system. You know, our immune system takes care of our colds and everything. But, like you said, the cancer just evades our immune system. So it's really, cool and futuristic actually to know that our own bodies can take care of cancer cells.

Dr. Cohen: Right, absolutely. And, and the truth is, you're exactly right, that it is your own body. And so the way that the CAR T-cells are produced is that we actually collect cells from the patient themselves. And so they, go through a procedure called apheresis where we withdraw their T-cells; and then they're sent off and engineered in a fashion that, that allows them to target the cancer. And then they're infused back through an IV infusion. So you truly are, in every sense of the word, using your own immune system to attack the cancer.

And the other thing that's really exciting is that often these cells remain in the body; and the, the hope is, is that in the long run, if the cancer ever tries to start coming back, that there will still be some residual cells that can reactivate and take out the cancer again.

Lizette: That's great.

Alicia: No, that is awesome and we actually encourage our listeners to be sure that they subscribe to our podcast so they don't miss our other episodes about CART. We'll be talking about other factors and other variables regarding this process.

On today's episode, we'll be speaking more so about, the side effects of CAR T-cell therapy. The first patient to receive CAR T therapy was treated in the US in 2011; and since then, several hundred people have received the treatment. Now although, like you said, CAR T's a great option for many, there are side effects associated with it as well, and many are severe. What are those side effects, of CAR T-cell therapy?

Dr. Cohen: Like any therapy that we administer in oncology, there is great promise but also, unfortunately, several toxicities and side effects that we have to monitor for. For most patients, the highest-risk time is the first couple of weeks after administration of the CAR T-cells; and there's a handful of, of now well-described side effects or toxicities that we look for and that, fortunately, we're getting better at managing.

One of the most severe toxicities is a syndrome called cytokine release syndrome or CRS. And what we think happens in this case is that when the T-cells are reinfused into the patient and, the immune system is activated, which is what we want. We want the immune system to be activated and take out the cancer. But sometimes it gets overactive, to the point where it causes a systemic inflammatory reaction that actually looks a lot like an infectious syndrome called sepsis.

So, for any of you that may be familiar with sepsis or have heard about it, what happens in this setting is that patients develop high fevers, low blood pressures, high heart rate. Sometimes they can have difficulty breathing, and it really does look like the patient is having a severe infection; but we know in this case that more often than not it's just a toxicity of the CAR T-cell infusion.

This can be or is a life-threatening side effect. Patients often have to go to the Intensive Care Unit and require significant intensive care, including ventilatory support and other medications to support their blood pressure. But, fortunately, we now have medications that are approved that can counter this and are typically very effective in shutting this process down within even a few hours of administering the medicine.

And so any center that administers CAR T is required to also have tositumomab, which is the therapy that we use to treat CRS. They're required to have that on hand, and we spend a lot of time training our staff, our ICU team, our emergency department,

and really anybody else who may come in contact with these patients in the first couple weeks after the infusion they're trained to recognize the signs of CRS and to intervene quickly.

Alicia: because of CRS being the most prevalent adverse effect, the FDA requires hospitals that use CAR T to have staff certified and trained to recognize and manage CRS.

Dr. Cohen: That, that's exactly right. So any center that is going to be approved to administer CAR T-cell therapy, both as, through the FDA-approved product or on clinical trial is required to have ready access to tositumomab. And, unfortunately, in medicine, emergencies like this often don't happen at 3:00 in the afternoon on a Wednesday. It's usually in the middle of the night on a Saturday night. And so we really take a lot of steps to make sure that night or day, weekend, holiday, or anytime, if there's a patient receiving CAR T-cells in the hospital, , that the tositumomab is available and that everybody knows where it is so that it can be administered within minutes if needed.

Lizette: And is it also like transplant? So many people, after getting an allogeneic transplantation, have to be, close to the hospital, just in case one of these side effects happens to them. Is this the same with CAR T if you're outpatient that you have to remain close to the hospital in case this happens? Are you still inpatient at this point?

Dr. Cohen: So every center handles this a little bit differently. But, in general, you're exactly right that any, regardless of where you're being treated, the expectation is that you are close enough to the center that's treating you that you could be back at that center within minutes, and so we require our patients to be within 30 minutes of our center as a condition of being able to be treated. And if they don't live that close, then we help them make arrangements for housing.

At our own site, we typically will admit patients for the infusion and have them stay in the hospital for the first seven days. And then if they're feeling well and not having any complications, they can potentially be discharged at that point to a location that's near the hospital.

What we know, especially with CRS, is that it typically happens within the first two weeks and even more frequently happens within the first five to six days. And so, for the most part, if you monitor a patient for the first seven days and they don't have any evidence of CRS, we tend to feel comfortable letting them at least leave the hospital

environment, with the understanding that at the very first sign of any problem that they will come back.

Often one of the first signs is a fever, but patients can progress from having a fever to being very sick within a few hours. And so anybody that has a fever during the first two weeks, regardless of where they are at the time, is required to, to come for emergent medical attention.

We also give patients a wallet card that they take with them so that if they happen to not be as close to Emory as we'd like them to be or something happens where they're out and they need immediate help, they have a card that says, "I'm a CAR T patient. I received my infusion on this date, and here's a number to call," so if they happen to end up in an Emergency Department somewhere else, so that they can get in touch with us right away. But, we work, we take a lot of steps to make sure that the patients are close by so that if anything does happen, we're the ones that they go to and can get them taken care of.

Alicia: And it's also good to hear that your hospital will provide accommodations for housing. I think it's really important for patients to hear that that type of service is offered. Any help that you can get to make this process less stressful, I think, is a great thing for patients to be reminded of.

Dr. Cohen: Sure. Well, and, unfortunately, we don't necessarily have a hotel on site, but we do have access to a Hope Lodge, where patients can stay. And often it's nice because many of our cell therapy patients stay there when they get discharged from the hospital; so there's an opportunity for them to potentially get to know other patients that are going through the same process. And then we do have social workers and other staff that work with patients to help secure lodging if the Hope Lodge is either unavailable or for whatever reason isn't an option for that patient.

Lizette: Yeah. There's a lot of support needed.

And just the support needed around a person getting a transplant, I think we're seeing the same thing with CAR T-cell therapy which it, it's new. It's something that, like you said, it has really the potential, if it's going to stay in your body, it potentially can be curative for people. But at the same time, you still need a lot of support, you know, before and right after getting this.

I know that that we just spoke with a CAR T-cell, recipient; and he's doing excellent now, and we're so happy for him. But he did tell us about the rough time that he had right after receiving his CAR T-cells. So, a lot of support is needed.

Dr. Cohen: Right, absolutely. And, and I think the, the transplant reference is, is a good one. So we, talked a little bit about CRS; and that's something that is a little bit more cut and dry in that patients have a fever or they have abnormal vital signs, and they're trained to come right, to come right in.

But one of the other toxicities that can develop is neurologic toxicity, and sometimes this can actually be subtle at the beginning. And so we, we truly rely on the patients and, and not only them, but their family members and caregivers to be very vigilant about identifying some of the more subtle neurologic toxicities that can potentially lead to more severe side effects.

And so we train the caregivers to be on the lookout for any sort of unusual behaviors or unusual speech. And, in fact, we often will have them administer questionnaires on a daily basis and other, do other more formal assessments each day to make sure that the patient isn't having the development, symptoms because, again, this can sometimes be a little bit more subtle. And somebody that doesn't know the patient as well may not recognize that something's going on.

One example, we had somebody who was an engineer who was going through CAR T-cell and looked well and, and to talk with him you wouldn't know anything. But their family noted that they were having a lot of difficulty with math and simple math that normally would not be a, a problem for them. And that was one of the first signs that we had a developing neurologic toxicity; and that patient ultimately ended up having a more severe toxicity that we wouldn't have been prepared for had we not recognized that something was developing.

And so we really truly rely on the caregivers to help us. And it doesn't mean that they, and sometimes there's something that comes up that we do a good assessment; and it turns out that everything's fine. But to at least speak up when they do recognize something out of the ordinary, because often that's the first sign that something's going on.

Alicia: Right. And do you find that patients are hesitant to kind of share theirs, I mean, of course, if it's a serious side effect that they, you know, have no, no choice in the matter.

We speak with doctors who say that when they put the patient on a new drug, because they, they appreciate that treatment, they don't want to say too much that will have the doctor do anything. Because in their minds they're getting the best treatment. They want it to work. So do you find that same hesitancy when it comes to CART?

Dr. Cohen: Sometimes we do. You know, one of the differences with this particular therapy is that it's, at least right now, it's administered one time; and so there's not necessarily the question of, well, do we need to continue it or what, are we going to do there?

Sometimes though the patients don't pick up on it or they, try to, explain it away and just say, "Oh, well, maybe I was tired or I just got confused for a minute." And so that's why we also do rely on more formal objective assessments, because you also don't want to have a situation, you know, where maybe a loved one says, "I'm really worried that they're not quite themselves," and the patient says though, "No, I'm, actually doing fine." And then you don't want to cause tension or something along those lines.

And so the way we often handle a scenario like that is just to have, a member of the staff who knows the patient well, you know, do an additional assessment to see if there have been any changes. And these are assessments that we do frequently, and so you can actually track how a patient is doing and if there's been any changes from the day before or even from a few hours before.

The other thing is that some patients that are particularly savvy and have done some of their research recognize that some of the therapies that we offer for patients with CRS or with neurologic toxicities are designed just depress the immune response.

And so, for example, patients with neurologic toxicities that they get severe enough are often treated with steroids. And when this therapy was initially developed, there was concern that administering tocilizumab or administering, administering steroids might blunt the impact of the CAR T-cells. And so that is something that's come up that patients are nervous about receiving something like steroids because they don't want to impair their outcome.

And, fortunately, at least in the studies that have been done so far, we have not seen a significant impact on efficacy, with the use of these supportive therapies. And so we work very hard to remind patients that the most important thing that they can do them and their caregivers, is to be mindful of their symptoms and signs that develop and let

us know so that we can try to intervene before it becomes a more life-threatening situation.

Lizette: Now can these neurologic toxicities be permanent, or is it something that, with time, will gradually get better?

Dr. Cohen: Fortunately, the overwhelming majority of patients will have their toxicities resolve. And so that's, and, and the same with the CRS. Fortunately, both of these are relatively short-lived toxicities. Now I, I think admittedly we, we don't have the long, long-term follow-up yet. You know, we're, we're still fairly early on n the development of this therapy.

And so we, we may find out down the road that there's some additional side effects that aren't quite as apparent at this point. But the, the overwhelming majority of patients that we've cared for at our center, whether they've ended up in the intensive care unit or had a more modest toxicity profile have recovered fully and have not had any residual deficits.

Lizette: That's good to know.

Alicia: I was speaking with one doctor; and he said, "It seems as if all my patients are coming in and asking for CART, because they just, they read about it, they know it's something that's working, and so it's this idea that, you know, try it on me. Let's see if it can cure mine as well." the comment that he made was, "This isn't a one-size-fits-all."

So how important is that for patients to know going into conversations about CAR T with their doctor?

Dr. Cohen: Right. Absolutely. I think that's a really important question. So there's no question that this is a very exciting new therapy. Right now, most lymphoma patients are actually not candidates for this treatment, at least outside of the setting of a clinical trial.

And so at, at this point, the therapy is only available, commercially for patients who have relapsed or refractory aggressive B-cell non-Hodgkin lymphoma. And even within that, there's a few caveats. And so many patients are not candidates for this type of therapy.

Now having said that, there are a number of studies looking at other lymphoma subtypes, like mantle cell lymphoma, and there's been work done in chronic

lymphocytic leukemia; and there's a number of other areas where we're investigating it.

What I often try to remind patients though is that although it's a very exciting new therapy, that there are definitely side effects and that there's a number of, of diseases out there for which we have well-tolerated, effective therapies where jumping right to CAR T may not be in their best interest. It might expose them to side effects that they don't necessarily need to take on right now.

And so I always think it's great when a patient asks about it, and certainly if we have a clinical trial available that they qualify for, I think it's always a good idea to think about going onto a study. But it's important for patients to remember that at least right now it's still in the investigational phase for most settings, aside from the specific group of patients with relapsed-refractory aggressive lymphoma, that have, that have relapsed after, usually after an autologous transplant or at least after several lines of therapy.

But again, I think asking your doctor about whether there are immunotherapy options is always a good idea. Just be mindful that it may, it may or may not be in your best interest at that time if there's a well-tolerated therapy that's available that we think is also going to be highly effective.

Lizette: And I think right now, it's really for relapsed or refractory settings, I know there's been some talk about first-line therapy. We still do have people that have CLL that are on watch and wait asking if they can get CAR T at this point.

So is that in the future first-line therapy, meaning not for somebody in a watch and wait protocol, but for somebody that might not have to have a relapse?

Dr. Cohen: So I think that's a great question and certainly is at the top of a lot of people's minds. I think that we would love to have a scenario where somebody has a B-cell malignancy or any malignancy for that matter and be able to administer an immune-based therapy to them and feel comfortable that it's going to eradicate the disease and they may not need any additional treatment.

I think we're probably still a little ways away from that scenario and, again, you know, I point out that, that these therapies are not without side effects and that, to be honest, we still don't fully understand some of the long-term side effects.

But, the idea is certainly appealing; and I think any of us that, that work in this field would love to be able to offer something like this that's a one-time therapy with the expectation that many patients wouldn't require any additional treatment in the future,

but still I think a little bit, a little far away till we get to that point. But I think it is likely to move up a little bit earlier on in the course of therapy.

So right now, for example, patients often have to have had a couple of relapses before they may meet criteria to receive treatment. It would be great to be able to offer this maybe earlier on at the time of first relapse or as a consolidation or sort of an add-on therapy for patients maybe with high-risk disease to try to prevent relapse. But those are all studies that are in development, and I think five or ten years from now the field may look very different.

Lizette: Yeah, it's already different from, you said seven years ago, right, Alicia, the first person? It's already so much different now.

Alicia: Yeah, yeah.

Dr. Cohen: Absolutely. It's amazing how much things have changed. I remember even at our own site, when we decided that we wanted to move forward with offering CAR T, we had to have a sit-down with some of the hospital leadership just to help them understand what it was and why it was important.

And now, you know, I think anybody that's involved with managing cancer patients has at least heard about this technology in some fashion; and there's a lot more familiarity than there was even a few years ago.

Alicia: We were speaking with a family whose son, Austin, was diagnosed with ALL at the age of five, right, Lizette? Was it five?

Lizette: I believe so.

Alicia: He had relapsed so many times. They were told there were no options. You know, they, and as a mother and a father, like that's such unbearable news to hear. But it is, exciting to know that science is progressing in a way that's allowing more options for people who are told there's nothing else we can do.

Dr. Cohen: Sure, absolutely. Even, you know, a couple years ago, there's patients that, now that we've treated that are doing well; but that if I would have seen them two or three years earlier, they may have come, and we wouldn't have had an, an option for that patient or at least not an option that we felt good could result in a long-term remission.

And it's a real testament to the, you know, to a lot of hard work by a lot of people that we're now at a point where this is something that can be offered and, again, is not a guarantee of cure for everybody but certainly gives patients and, a therapy that we can be optimistic is going to provide benefit for them.

Lizette: Very hopeful.

Alicia: CAR T began as a clinical trial; and, like you said, CAR T has been approved to treat two cancers to date. However, we're seeing clinical trials in which it's being used to treat other cancers to determine its effectiveness, like myeloma. And many hear the word "clinical trial" and are hesitant to ask their doctors about it due to many myths that have been, that have managed to pass through the years, either get those people who are like, "Yes, let's try it." And you get those other people who are like, "I don't trust it. How important are clinical trials?

Dr. Cohen: Yeah, so I really appreciate you bringing that up. I think that, CAR T therapy is the perfect example of where clinical trials are just so important in the development of new therapies. And, and to your point, I often have discussions exactly like what you described with patients. So we have some that come to our center because they know that we have clinical trials to offer, and they want, you know, whatever is, is new and exciting. And then there's others that even if they may be a great candidate for a study are concerned about the potential risks of going onto a study.

And, unfortunately, I think there is a little, a degree of mistrust in some instances where patients feel that maybe we are, quote "experimenting" with them or, or treating them like a, a guinea pig or, you know, things like that. You know, sometimes patients will, say that, you know, "Well I don't want to be a guinea pig." And I think what's important for people to recognize is just what goes into the development of a clinical trial.

Before it ever gets to the point where a, where a patient could potentially be treated, and so there's often years of, preclinical work that's done in the laboratory without patients, maybe using patient samples but without actually treating patients to first, you know, develop the technology and, and make sure that it works in a fashion that they expect it to work.

And then in order to actually get to the point where you administer a therapy to, a patient, there's a number of layers of regulations that ensure that patient safety is being taken into account at all steps. And the FDA, has oversight over pretty much

every clinical trial that gets conducted in the United States. And then each institution has something called the Institutional Review Board or the IRB, which reviews every single therapeutic protocol to make sure that patient safety is being considered and that it's an appropriate study to do.

And I can tell you as somebody that writes studies, that there may be scenarios where you initially want to incorporate a treatment or some particular assessment into a study. And maybe at the time that you're developing it, it seems reasonable. But then when you have sort of the multidisciplinary group like an IRB that includes often patients and physicians and scientists from around the institution they may look at it and say, "You know what, it doesn't really make sense to do that in that situation because I'm, they're concerned about it being a potential issue for patient safety."

And so then we work together to figure out how can we answer that question in a safer fashion? And so there's a number of times that clinical trial protocol goes through this sort of oversight before it ever gets to patients.

And then during the conduct clinical trial, we are monitored very closely by a number of different agencies to ensure that we're adhering to the protocol in the right fashion. And if there happens to be a deviation or a situation where something doesn't occur according to the protocol that's often discussed with the IRB; and we work hard to make sure it doesn't happen again.

And so there are a number of measures taken to ensure patient safety; and then even sometimes if, if a protocol is being conducted properly, but there is some sort of an unexpected event, there are a number of steps that are taken, including potentially stopping enrollment, or amending the protocol to make sure that future patients aren't exposed to the same risk.

And so, I think that it's important for patients to recognize that their safety is at the top of the priority list for every single person involved with it, with the conduct of a clinical trial. And then beyond that, I think it's important that patients recognize that this is really how the new therapies are developed, and pretty much every therapy that is FDA-approved for use in the treatment of cancer patients has to go through a clinical trial process. And this is often a, a way that patients in a very controlled, monitored environment can, can have access to some of the most exciting new therapies for their disease.

Alicia: Absolutely. And it's so important for, for our listeners to hear that because there's so many myths about clinical trials that have been just passed through the

years. And so I think it's very important for them to hear from a physician how controlled it is and how this is something that they're not just thrown into a situation; but conducted in a way that follows guidelines. It's one that allows them to feel at ease that they're being given the best care. So I think that's, that's very important to know, so thank you for that.

Dr. Cohen: Oh, absolutely. and it seems a little bit extreme, but I often will tell patients, you know, whenever we're discussing a study, you know, I don't worry. You know, this isn't something that I just sort of developed, you know, in the back room ten minutes before you came in.

Dr. Cohen: I try to help them understand that, any time we offer a therapy that's on, in the setting of a study or an investigational therapy that there is rigorous training for all people involved and, and a very thorough process to make sure that, that the patients are going to be kept safe. In addition to the medical care that we provide, that there's so many other personnel involved, both at our institution and nationally to make sure that it's conducted properly.

Alicia: That's wonderful, thank you.

Doctor, when you're speaking to patients about CAR T and for those patients and caregivers that may be listening, what are a few questions that you would suggest that somebody ask about this process? About side effects?

Dr. Cohen: So, I think it's really important, for patients to have a good sense of how the process works at that individual institution. And so there are a number of different ways that it can be set up. So sometimes most of the therapy is done as an outpatient. Sometimes it's done as an inpatient. Sometimes patients have to stay in the hospital for seven days. Sometimes it's longer. Sometimes it's shorter.

I think having a realistic understanding of what the, what it's going to actually look like so that they can start to make plans for when they may need a caregiver to be present, how long it may take between the, that initial consultation when they may decide to move forward, and the actual apheresis and then subsequent treatment.

These are all things that we try to address at the time of the initial visit because certainly the decision to use CAR T from the medical standpoint and from the standpoint of the disease is one thing. You know, deciding that that's the right treatment. But the other thing that I think is equally important is helping patients understand well what does that actually mean for me and for my life.

So, you know, we're in Atlanta; and so many of our patients come up from South Georgia or from some of the neighboring states. And for them, it's really important that they know early on what is going to be involved, when will I need to be in Atlanta, how long will I need to be there, where, where will I stay? Those types of things, so we try to get that process started early on.

I think the other thing that's important for patients to talk to their doctor about is sort of what the follow-up is going to look like and what they expect may be some of the long-term issues that they'll need to deal with even after they leave our site.

And so one such example is that many patients will have low antibody levels. So when the CAR T-cells target CD19, it can also take out the normal cells that ultimately grow up to develop, to produce antibodies. And so some patients will need to have antibody infusions for potentially months or even years afterwards, and that's typically done, something that can be done locally. But these are things that it's important to start thinking about early on to make sure, for example, that you have an oncologist locally that you can work with, , and that you have the support you need, in your own community to potentially be able to handle any of these types of things that come up.

And then the last thing I think that is always important is that although CAR T is very exciting. I think it's always a good idea to talk with your doctor about what else is available. Are there other clinical trials that may be available? Are there other therapies that may not be immunotherapies or may be a different type of immunotherapy that may actually be a better option for one reason or another for you as opposed to CAR T. And so just because CAR T is one option doesn't always mean that it's the best option. And so, I always try to have a discussion with my patients, even those that come specifically for CAR T, to try to help them understand why is CAR T most appropriate for them and what else, what other options have we considered before we make a decision?

Alicia: That's great advice. Thank you so much.

Well thanks so much for joining us on today's episode, Dr. Cohen. It our hope that the more that is learned about CAR T's incredible work from researchers like yourself, it'll allow for toxicities to be anticipated and manageable, allowing for improved quality and universal benefit.

We'd also like to thank Celgene, Kite, and Novartis for their support of this episode; and for those who would like to read more about CAR T-cell therapy and clinical trials and other disease-specific resources, you can visit www.lls.org/booklets and download

and print our booklets free of charge, as well as a one-page document we have that outlines the entire process of CAR T.

So thank you, again, Dr. Cohen. You shared such great information. We know our listeners will benefit from it as well.

Dr. Cohen: Oh, absolutely, it's my pleasure. And I appreciate the opportunity to speak with you about this really exciting and important topic.

Alicia: Thank you.