LEUKEMIA & LYMPHOMA SOCIETY®

THE BLOODLINE WITH LLS

A PODCAST FOR PATIENTS AND CAREGIVERS

Episode: 'Innovative Therapies for Acute Leukemias'

Description:

Join us as we speak to Dr. Hongtao Liu and Dr. Adam DuVall from University of Chicago Medicine, about current and emerging cellular therapies for acute leukemias. These innovative therapies include CAR T-cell therapy, modified Natural Killer (NK) cells and stem cell transplantations. In this episode, we discuss how these groundbreaking therapies have changed the landscape of treatment for acute leukemias. The doctors share what they are excited about in the future, citing how clinical trials are advancing therapies and how cancer centers can better serve the unique needs of adolescent and young adults (AYAs) with acute leukemias by utilizing a holistic and comprehensive approach.

Transcript:

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

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

Elissa: Today we will be speaking to Drs. Hongtao Liu and Adam DuVall about innovative therapies in leukemia. In addition, we'll hear about how adolescents and young adults can benefit from additional services to guide them through age-related unique circumstances.

Dr. Liu is the Medical Director of the Clinical Cellular Therapy Lab for Hematology/Oncology and an Associate Professor of Medicine at the University of Chicago. He specializes in the diagnosis and treatment of leukemia, stem cell transplantation, and cellular therapy. Dr. Liu aims to develop novel therapies to fight leukemia and prevent disease relapse.

Dr. DuVall is a hematologist/oncologist at the University of Chicago Medicine, specializing in the diagnosis and treatment of care of adolescents and young adults,

commonly referred to as AYAs with an emphasis on acute leukemias, lymphoma, and complex cancer predisposition syndromes. As part of the University of Chicago Medicine's Adolescent and Young Adult Oncology Program, he provides comprehensive cancer care to AYAs through collaboration with a multidisciplinary team. His research includes exploring novel therapies in leukemia treatment and how to decrease the impact of cancer therapy on psychosocial development of AYA patients.

Welcome Dr. Liu and Dr. DuVall.

Dr. DuVall: Thank you for having us.

Dr. Liu: Thank you very much.

Elissa: So let's start by learning a little bit more about each of you. How did you both get started in medicine and study in leukemia?

Dr. Liu: So, my decision to medicine was influenced by my parents. My parents are doctors in China. I was very interested in biology, but they convinced me to go to medicine. I thank them very much. I enjoy the medicine, so I think to help people to treat a disease, especially a very, very bad disease like leukemia.

Dr. DuVall: I came to a bit of a circuitous route to medicine. I was interested and good at science, but I also actually studied comparative theology and did a lot of different artistic things and was applying to graduate programs in theology in addition to med schools. Then I took some time off after undergraduate and helped to run a free clinic in a poor area of Indiana; and that really influenced my want to go into medicine.

And then in med school, I thought I was going to be the next Paul Farmer, who, unfortunately, just passed away last month and was working in Kenya and doing a lot of work in parasitic infections and how they affect the immune system and how they affect the patients.

I got really interested in the immune system, and then my wife took a job with St. Baldrick's, which is a program that does a lot of head-shaving events and things like that. And so I started going to her events and really fell in love with the population, and it really fit well with my interest in the immune system; and then the care of the underserved kind of got me into taking care of adolescents and young adults with cancer, which are a relatively underserved population within the cancer community. So all of that kind of led me to where I am now and I am very happy that I ended up here.

Lizette: Sure. And I know that the AYA community, especially in our blood cancer community, is an underserved population. So we're glad that you are bringing them to the forefront of your studies as well as treatment for AYAs.

Now Dr. Liu, you run the Clinical Cellular Therapy Lab at the University of Chicago. Can you tell our listeners what cellular therapy is?

Dr. Liu: Yeah, I'm the Medical Director. Dr. Wickrema, actually is running the staff, but I'm providing medical advice. And the cell lab processes all the cell product including the stem cells from the patient. Cellular therapy is such a broad area. The stem cell transplant is the first cellular therapy, right, using the donor's stem cells. You're actually using donor's immune system. And, also, even post-transplant, we use some cells to control the disease or treat a disease relapse.

But the modern concept of cellular therapy is more likely using the immune cells. Most times it's the T-cells, and now you will mention about other cell types like natural killer cells, NK cells. The most attention right now is on the CAR T-cell, chimeric antigen receptor T-cells because that's approved for multiple indications, especially for lymphoid disease, like in acute lymphoblastic leukemia [ALL] and also lymphoma, multiple myeloma. We have a long way to go for other myeloid leukemias like AML, acute myeloid leukemia.

Lizette: So why is it so beneficial in leukemia and lymphoma patients, the CAR T-cells?

Dr. Liu: Yeah, so in order to do the CAR T therapy, you had to have a target for the disease, right? For the lymphoid disease, they have an excellent target of CD19 and CD20 or CD22. Almost all the leukemia cells. And the normal B-cells also has this target. You can argue that CAR T not only kill the leukemia cells, also will kill the normal B-cells, causes some immune deficiency.

But you can survive, actually without the B-cell, even low-level B-cells. That's why it's very effective. In the pediatric patients, sometimes you try to prevent infections we give them donor's antibody, IVIg, immunoglobin, try to prevent infection. In adult, actually we are not routinely giving a patient post-CAR T, IVIg, unless they have an infection.

So for myeloid disease, that's difficult. We don't have very good target. There's some target, but all the target like CD33, CD123 are also on the hematopoietic stem cells. Right, you can kill the leukemia cells if you kill the hematopoietic stem cells you can now survive. That's the difference. So we are working very hard to find the best target for myeloid lineage leukemia.

Lizette: Right, I know, Elissa, you were very interested in knowing more about AML.

Elissa: Yeah, I'm an AML survivor myself; and so I kind of keep up on what clinical trials are going on, and I have friends going through AML treatment right now. And I've noticed there are some CAR T trials right now for AML. Could you tell us about that, and do you see that as a possibility for AML patients in the future for CAR T?

Dr. Liu: Yes, I think that there is many, many clinical trials ongoing right now. the major target actually still are the target I mentioned earlier, CD33, CD123, also CR1. There are some clinical response. I think we are opening some CAR trials target the CD33. According to one report presented post-ASH (American Society of Hematology),

50% of patients had a response. Now we don't know how durable the response, and don't know can provide cure. It's a still question. Maybe you can bridge a patient go to the transplant, have disease control, go to the stem cell transplant for the eventual cure. That's possible.

We still in some early phase compared the lymphoid leukemia because of the target issue, but I think we are making some progress actually; and there's also other form, not only the CAR T-cells but also NK CAR, right, and also, even now there's some leukemia-associated antigen lymphocytes, and to control the disease relapse. Even in the future there could be a TCRT. There's many potential cellular therapies for AML, but we are still in the early phase. We saw some promising results but need to be confirmed in the larger studies, but I think we're still a little bit far away from any FDA-approved product in the near future.

Dr. DuVall: I think that what Dr. Liu said is really important, especially with all of the information that's getting out into just kind of the common space and news releases and things like that is that the hope of cellular therapy is really a cure for a blood disease. And as Dr. Liu mentioned, the first cellular therapy and the still most reliable, most important cellular therapy is using a bone marrow transplant. That is a cellular therapy; and it's still our most studied, our most effective, and our highest chance of cure in any type of leukemia.

I focus more on the lymphoid leukemia; and so we have been using CAR T for a few years. But even in that, we don't know the durability over 20, 30, 40 years. And it seems like some people will lose their CAR T-cells over time; and that durability might not equal cure. And so really, there's a question now of, after this type of cellular therapy is do you need our more traditional one that we have decades of experience with? And especially for young, healthy people, we know for a fact, with it, because of these decades of experience can lead to a potential cure, whereas we're still uncertain for some of these other novel therapies while they're still very important and really are

an amazing therapy. They do lead to some other questions that I think we still need to answer.

Elissa: Now a question. You were talking about stem cell transplant for ALL. For that we do allogeneic transplants or getting stem cells from a donor vs an autologous transplant, which is using a patient's own cells. That type of transplant is often reserved for other blood cancers like myeloma or some lymphomas. Could you tell us what the benefit is of using a donor's stem cells?

Dr. DuVall: Your immune system has a job of fighting infections and of preventing cancer in some ways. And so the immune systems of our patients with blood cancers is broken, and a lot of the ways we can kind of reset it and fix it, all with just chemotherapy or other types of treatments. But in some ways it's so broken that we know the cancer will come back unless we replace it with a new immune system that can then prevent the leukemia from coming back for, hopefully, a lifetime.

And so that is still a mainstay of treatment in acute lymphoblastic leukemia, ALL, which is what I more focus in; but see everybody with any type of acute leukemias.

And that's now, in some ways, luckily, only reserved for people who have very high-risk disease and who become refractory to therapy or who have relapsed. In acute myeloid leukemia, it's much more common and needed; and I think there are much more needed therapies for this. But I can let Dr. Liu speak to that because I think he has a lot more expertise in that area.

Dr. Liu: Yeah, I totally agree with Adam. I always tell the community oncologist, stem cells is immunotherapy, is a cellular therapy, has been there for several decades. This is still the early cure for many leukemias, especially for AML, acute myeloid leukemia, especially with high risk.

The allogeneic stem cell transplant we use in the donor's immune system. That's why it's an immune therapy; and there's autologous stem cell transplant for some low-risk

AML, but we are not using a lot. That should just give the chance, very intensive chemo to eradicate the leukemia. But allogeneic stem cell transplant, even while using different conditioning, we're using myeloproliferative conditioning in the past, try to eliminate some cancer cells, but right now the stem cells transplant, actually, is using the immune system from a donor try to control the disease. And the stem cell transplant is still the early cure, even with available all the cellular therapies. I mentioned early we are using several therapy to bridge a lot of patients with relapsed-refractory disease to transplant because the disease status before stem cell transplant is very important. If you go to transplant with active disease, you will have very higher chance to have relapse.

Lizette: I think that was my question, and I don't know if we have a total answer yet because CAR T-cell therapy is newer. But is CAR T-cell therapy always a bridge to transplant, or is CAR T-cell therapy going to actually replace transplant in the future? What are your thoughts?

Dr. Liu: Yeah, that's a good question. I can start, and I think Adam can add more, because he has more experience in the lymphoblastic leukemia. With some long-term follow-up, about 40%, patient could have some long-term survival with long-term follow-up. You could argue this kind of patient could be cured with CAR T. Right now, the researchers try to develop some biomarkers how to determine which patient that can be cured, have long-term survival without stem cell transplant.

Most other countries, even the researchers in China, most of the time they use CAR T-cells as bridge, then go to transplant because in that situation this can cure more patient. But I think we need a lot more research to determine which patient could be cured with CAR T-cells alone, which patient could use CAR T-cells as a bridge to go to the stem cell transplant for eventually cure. But even with stem cell transplant, relapse is still the problem. Actually, I think we tried to develop some new strategy, try to make cellular therapy strategy to prevent relapse, even after stem cell transplant.

Dr. DuVall: Yeah, I really agree. I think there is a subset of people that are cured with CAR T-cells. I don't think we know exactly what that subset is yet. There is some work now, and Dr. Liu mentioned this earlier, the CAR T-cells also kill our normal B-cells. And there's a good amount of work out there now that shows that most of the time, I don't want to say all the time because in medicine you can never say all the time, but we will be able to detect normal B-cells coming back before any type of relapse of the leukemia.

So there might be an opportunity, and this is something to think about for young people, that if they've already had a transplant or if they're very sick from their disease or from the CAR T-cell or for something, it is reasonable just to watch them for a time period and could be for years is kind of the unfortunate thing. And look closely to see if you can see any normal B-cells.

And then it's pretty reliable that after normal B-cells come back, a relapse of the disease is very likely. So, you do have potentially a small window that you can have without any detectable disease that you could potentially go to transplant if, the B-cells come back. That's, again, a little tough to perfectly, thread a needle, but it's a possibility.

Or, you know, there are so many different ways of returning people into remission now with acute lymphoblastic leukemia that you can also just wait and see approach. But, with each decade after CAR T-cell, we see it seems like slightly fewer people are in that, kind of tail. You see these survival curves that, I'm making a line now, but nobody can see it.

But what you're looking for my young population, and I'm a pediatric oncologist too, is you're looking for that plateau at the bottom. How many people stop relapsing after, 30 years? I don't know that we've hit that plateau with the CAR T-cells yet. I think it still takes another decade or so because like you've said, they're so new. So right now,

we're at 40 to 60% of people might be cured; but in ten years from now, we might be less than that. We don't know yet.

So there is a watchful waiting strategy. I will say for my young patients, including pediatric patients, if they haven't had a transplant yet, if they are fit and they have a reasonable donor, I think most people nowadays would say to go onto a transplant after CAR T-cell therapy because it still offers the highest potential of cure.

That's a tough discussion to have; and that's a tough decision to have. But, really, with transplant in general, all of our transplants, they're called elective transplants because they are elective. There's always options beside transplants. It's always weighing the risk of the transplant, which is higher than traditional chemotherapy, versus the benefits of it.

And so that is an individual discussion with each patient, that is not a perfect answer for anybody. But you can get general ideas; and some of it is patient preference. I've had patients who want to finish school or do other things; and watchful waiting does timeout with that, or I want to get married or potentially want to try to have a kid.

I actually took care of a patient who was, I think, one of the first patients to become pregnant after CAR T-cell therapy in the world. And it's something that happens. And so there's lots of individual decisions for that.

And so, I think it's a hard answer to have a general one to; but, if you're a young, healthy person, you haven't had a transplant before, you have a good donor, you'd have to have a really good reason not to go to transplant after CAR T-cells in my book.

Dr. Liu: Yeah, I totally agree with Adam. I can also give you an example for older patients. I have a patient, presented with relapsed refractory ALL at age 76. Not a transplant candidate, not necessarily from age point. No one wanted to offer the transplant, easily to such a patient and they're 76. We put on the CAR T treatment on

the clinical trial. Actually, he did very well, entered remission. Right now, so three years after actually, still in a remission.

Now, Adam also mentioned for young patient, we have better monitoring for the disease. You can always offer the transplant, know why you see early relapse, right, if the patient is not ready to go to transplant. But I totally agree, for younger patient, very fit, has perfect donor, now the transplant still can provide the best chance for the cure.

Lizette: Sure. And I know that our patients are always wondering about treatment sequencing, right? So, you can have CAR T-cell, and then you can have a transplant. Can you have CAR T-cell and then CAR T-cell again or transplant and then another transplant to follow?

Dr. Liu: Yes. I think a lot of patients enrolled on the trial actually had a relapse after their stem cell transplant. They got the CAR T-cell and their disease control, but not a lot of centers doing second transplant. Second transplant is getting popular. Now we do have a protocol, actually, and to perform a second transplant using different conditioning. They call the total marrow irradiation. Actually, we presented the data at ASH almost two years ago, and the outcome was very promising. We tried to publish the data.

I think the sequence is always difficult. A lot of times the patient has refractory disease. They failed all the standard treatment. Right now we're using CAR T-cells to treat the disease, put them in remission, and go to transplant. But there are also situations, you could have relapse after stem cell transplant, right? You enter the remission with the standard chemo. Now you went to the transplant. You had a relapse. Now you are using CAR T-cell to control the disease, and some patient also had a second transplant.

Dr. DuVall: And to add to that, Dr. Liu, actually is the primary investigator on a study here looking at cellular therapy for people who are MRD-positive, so minimal residual

disease-positive after a transplant. So we know that there's this low level of disease there, and those patients are much higher risk to have a true relapse; and, is there a role for either CAR T-cells, or like Dr. Liu mentioned before, these natural killer NK cells to be used after, prophylactically, to prevent relapse or if we know there's minimal residual disease, to prevent true relapse. And I think that's a future of the therapy as well, especially, potentially from the myeloid disease but, hopefully, in general.

From the lymphoid diseases, the order of therapy is the million-dollar question for these diseases now. Should we use CAR T-cells earlier on? Should we use them later? Should we use them only after transplant or if they're refractory?

We also have other targeted therapies in these diseases, including inotuzumab and blinatumomab, which target things that the CAR T-cells also target. So, should we be using those instead? But, yeah, needless to say, you can use CAR T-cells before or after transplant.

We don't have anything that I know of that's looking at prophylactic CAR T-cells, post-transplant to prevent relapse; but that would be a study that would be needed and could be very interesting. But for ALL, at least, it's not quite there yet.

There are two different types of ALL, B-cell and T-cell ALL. And all of these things that we're talking about, I just want to make sure I say it at least once is, is for B-cell ALL. Because with T-cell ALL, we are in need of some really good treatments for relapsed or refractory disease similar to AML because those targets that are for B-cell ALL aren't present in T-cell ALL, just like Dr. Liu mentioned for AML. So there's still a lot of need, not just sequential therapy, actually new agents as well.

Elissa: I'd like to go back for a second. Dr. Liu, you mentioned other cellular therapies like natural killer cells or NK cells. I'd love to hear about that, but also off-the-shelf CAR T therapy. Could you tell us a little bit about those?

Dr. Liu: Yes, yeah. It's a very interesting area. Let's talk of the off-the-shelf CAR T first. Right now, true that the CAR T - the product all using, they call it autologous lymphocytes from the patient. Sometimes recruited from real patients. Some patients had a transplant recruited from the donor, right? Some donor lymphocytes. But is collected lymphocytes from the patient. They do the engineer, right, to generate the CAR T-cells, so the time would take about three to four weeks.

But right now, this a new technology. They can get the product ready within days. Even over night, they have in vivo expansion. There's some new technology, but so far, all approved products actually will require a couple weeks for manufacture of the CAR T-cells. But sometimes patient cannot wait, right? The disease just progressed even while we include the patient on the trial, some patients last opportunity to get the CAR T-cells because the disease just too aggressive. They just died from the disease before they were able to get the CAR T-cells.

Right now, we try to develop some off-the-shelf, they're called allogeneic CAR T-cells. Actually, they're from lymphocytes from the donor. They had to do some more engineer because they have to not allow the T-cells from the donor attack the body, can cause GVHD, graft-versus-host disease. They have to do more gene editing to knock out some genes, especially the TCR-alpha gene, and in that case not causing the GVHD. There's also issues how sustain these CAR T-cells in the body, because the recipient's immune system has a tendency to gather it all for this, the allogenic CAR T-cells not like autologous CAR T-cells. Because the T-cells from your body will give some lymphodepletion, the CAR T-cell can stay there for quite long time. Some could stay in your body for years to control the leukemia.

But then another problem for allogenic CAR T-cells, actually, your body could eliminate these cells very quickly, now we have to fight the lymphodepletion regimen to allow these CAR T-cells to stay.

A lot of companies are developing different strategies; actually, we have with the trials here, a target CD20 and there's many other company try to using different the gene editing a different way and to do this, actually, I think it could be promising. At least in the lymphoma looks like they had some good result, but in the leukemia, especially for lymphoblastic leukemia I think we still need to see.

The second question is, NK, right? The immune cells, lymphocytes is the most important cells in the immune system, but there's other cells, like natural killer cells, right, they are very potent to kill, but they don't last long. They don't have memory. They have less toxicity. So right now, there's a lot of trials going on using the NK cells to generate the NK CAR. Actually, there's published data suggest that they could be very effective. Actually, very minimal toxicity. A lot of companies try to develop this CAR and we do have some trials and the NK CAR against the AML in our center is early phase.

We try to do some prevention of disease relapse infusing some half-matched NK cells and to the recipient try to treat a disease relapse. Right now, there's off-the-shelf NK product; actually, they can generate the NK cells even from the core stem cells, placenta, so they have a lot of NK cells, that the allogenic NK cells there that you're ready to use. We have a trial try to imitate the minimal residual disease in the AML settings, we have a trial to treat relapsed/refractory AML.

So I can give you example. I have one AML patients had a very complex karyotype, very high risk, and failed the standard of treatment. And the patient is a transplant candidate, but we cannot move to the transplant without decent disease control. So I put the patient on the NK trial. Actually, the NK cellular therapy was able to control the disease, and the patient was able to move to stem cell transplant.

Elissa: Oh that's interesting. Now you talked a little bit about side effects for the natural killer cell treatment. What about for CAR T therapy? Are there many side effects that come along with that?

Dr. Liu: Yeah. I think it's two side effect that everyone is talking about. One is the CRS, cytokine release syndrome. The other was the neurotoxicities could be very bad, and right now we know better how to deal with this.

Now we have one better strategy, and we can actually intervene early. Right now, actually, in our center, we didn't see a lot of high grade with the CRS or neurotoxicity. And the advantage for the NK CAR because of they are very transient, actually, they disappear very quickly. They just kill the leukemia, lymphoma cells then they disappeared. Actually, the incidence of the CRS neurotoxicity is very minimal or much less compared the standard CAR T-cell.

Elissa: Oh, that's really good to know. Now we talked a lot about all these different cellular therapies, which is really exciting. You did mention a little bit about some clinical trials going on, but I'd love to know what's on the horizon right now? What are you each really excited about that you're seeing either in trials or being talked about?

Dr. Liu: I always tell the patients, also physicians, "The best treatment for the leukemia, especially AML, acute myeloid leukemia, is a clinical trial." Either, the novel agents, target agents, or even cellular therapies.

And from a cellular therapy point, we try to develop some NK CAR or regular CAR T-cells for the AML NK CAR and also, we try to do all of us some, you know, leukemia specific antigen and cytotoxic lymphocytes and to treat a disease relapse or prevent a disease relapse. So, we try to find the best way to treat the relapsed/refractory disease. That's most unmet need in the AML settings. Maybe in all the leukemia settings.

Dr. DuVall: I think a lot of the exciting trials with cellular therapy in the lymphoblastic leukemia space are looking at better ways to do it. So, there's different constructs, different ways to make CAR T-cells that could potentially lead to higher rates of cure that eventually avoiding a need for an allogenic transplant.

There are also things that are out there that are kind of being able to turn on and turn off the CAR T-cells, which would be a really interesting ability to do so to prevent, long-term harm or to reduce the toxicity in the easier way.

And then, really, it's the new targets, I think, for a lot of the ALL specifically just like what Dr. Liu mentioned. We need targets for T-cell ALL. We don't have them. They're commercially available. And we need targets that are going to work for ALL that loses the targets that we have currently. We have a lot of targets for ALL currently on the B-cell side, but it doesn't work for everybody. We're still losing people to leukemia and so we still need further developments on that.

So between making better CAR T cells that are going to work better and cause less toxicity or potentially avoiding late effects from transplant, or looking for new targets in these spaces is really, I think, what the next step is.

Elissa: Yeah. That's really great. I love to hear about the new things being talked about and seeing where we can go, particularly when you're looking at relapsed or refractory that really need that help that they're not getting that response on the first-line treatment.

Now, Dr. DuVall, we mentioned in the introduction that you are part of the Adolescent and Young Adult Oncology program at the University of Chicago Medicine. And as some of our listeners may know, acute lymphoblastic leukemia, or ALL, is the most common childhood cancer, so we would kind of expect to see young adults dealing with that. But young adults are also getting diagnosed with acute leukemias. I was diagnosed with AML at 34. But the AYA cancer community has some pretty unique characteristics that aren't as relevant to the pediatric and elderly cancer populations. Could you share what makes this subset of cancer patients unique?

Dr. DuVall: Yeah. And I appreciate that question. The type of cancers that are seen in the AYA population are unique. ALL is probably the most common one that we think

of from the blood cancer standpoint, but AML is also very common, and they both require kind of unique therapies for this age group.

AYAs are kind of caught between being an adult and child and that's both true in life with the journey from living with your parents and then gaining independence and consider AYAs in the United States to be from ages 15 to 40, so you can tell there's lots of development that goes on during that time. You transition from, like I said, childhood to adulthood and that comes from not only a financial standpoint, including insurance coverage, and also from job, career, schooling, all of that standpoint but also from a psychosocial standpoint. So the ability to form adult long-term relationships, whether they be friendships or romantic relationships, also sexual development happens during that time. And all of that is horribly impacted by cancer and its therapy.

So we know already that we don't do a good job in medicine of taking care of that side of things. And part of that could be because it's either being taken care of in a children's or an adult hospital, which is very separate. And I actually did training in both pediatric and adult oncology because I wanted to learn both perspectives and I wanted to get both points of view, and they are different. Neither of them are perfect and neither of them are perfectly right for every individual. So I think it takes a unique team to be able to take care of these patients and a different focus to be able to help them.

There's actually a great book that was published, I think, last year. It's called *Between Two Kingdoms* that probably a lot of people have read that was written by a patient who was young and had AML, similar to yourself, and underwent a bone marrow transplant, and really speaks to the unique challenges that somebody who's young with cancer faces in developing, mature relationships and all the other stuff that is happening to a young person when going through cancer and it's therapy that isn't addressed by a lot of doctors and by the medical system as a whole.

Elissa: Yeah. I definitely see that young adults end up kind of having to figure out their own way a lot of times. And LLS recently came out with a Young Adult Survivorship Workbook to, hopefully, kind of help them through those, but I think it's great that young adults are starting to get a lot more attention because those unique issues do need to be addressed.

Now there's something I want to touch on, and its young adults with ALL. There's been a lot of talk about doing pediatric versus adult protocol. And a lot of times if they're just barely outside the pediatric range, up to 18, and they're not seeing their pediatrician, they might not get that pediatric protocol for ALL treatment. Could you kind of go over that a little bit?

Dr. DuVall: Yeah. So I'd take a step back a little bit too. ALL is a rare disease in general, so even within the cancer community, it's a rare disease and likely should be treated by somebody who specializes in the treatment of acute leukemia and ALL specifically because it is such a rare disease.

There is a lot of work that was done by one of the people that started the AYA program here at University of Chicago named Wendy Stock who really has shown and revolutionized the care of young people with acute leukemia and this area acute lymphoblastic leukemia that has showed that there is seemingly benefit to using pediatric-based protocols as opposed to adult protocols up until the age of 40 at least and potentially longer.

We published not too long ago that it's safe to use these pediatric-based protocols in older populations up until the age of 60 with some modifications, but at least up until the age of 40 it's that we can mimic pediatric pediatric-based outcomes in the adult side using the pediatric-based protocols whereas before there was a deficit of outcome. People who were treated by pediatricians and who are the same age seemed to have better outcomes in the adult side, which was corrected for by switching the type of protocols we use.

And that is difficult. These protocols are very involved. They're very unique. And there is some data out there that in certain centers that the traditional adult protocols can be about equally efficacious, but they haven't been really replicated outside of those centers, so the kind of go-to treatment for ALL if you are an AYA should be a pediatric-based protocol, hopefully, in a clinical trial because we are always trying to improve outcomes. But at minimum, having somebody who's an ALL-specific physician or at least see the patient and help out with therapy is really I think a necessary thing because this is a very rare cancer that is just not seen in this population very frequently.

Dr. Liu: Yeah, I totally agree with Adam. Dr. Stock started the program. Actually, it's very successful to deal with this special population. They are very difficult to deal not of only from disease point, also from a psychosocial point and this program help us a lot. And I treated several young patients in the past. Actually, right now we always refer this kind of patient to the clinic and the program. They are doing a wonderful job to treat this kind of patients.

Lizette: Great. So Dr. Stock did start this program at the University of Chicago and some of the larger cancer centers have separate programs for AYA cancer patients. Can you just tell us a little bit more about the University of Chicago's program and how it benefits adolescents and young adult cancer patients, Dr. DuVall?

Dr. DuVall: Yeah. I'd love to. Obviously, I love talking about our program, and Dr. Stock is one of the reasons why I'm in Chicago. I did my training out on the West Coast with the Oregon Health & Sciences [University; OHSU], which is one of the first AYA programs created by Brandon Hayes-Lattin who's really revolutionized the field as well. And so, there are a lot of different AYA programs. Everyone is very different.

In our program, we focus on the treatment of adolescents and young adults with any type of leukemia. Now that I'm here, I also see lymphoma, so any type of blood cancer and you're less than 40 can come see us in the AYA program. And I would see

all the patients with lymphoma and, actually, Dr. Stock and I take a team-based approach. So we're effectively, one person. We both joke that we share one brain because we spend so much time together at this point that, they'll be in clinic and they'll either see myself or Dr. Stock, and it just depends who's there.

So it's a program that really runs independently of either of us because we're both either on inpatient service or she's out traveling the world, hopefully soon, now that it's opening back up, teaching the rest of the world how best to treat this type of disease. And so it's a real team-based approach from that standpoint. So we take the active role of being a treating physician for those subsets of patients, and we have a multidisciplinary team, including palliative care. We actually have an AYA program administrator who's a licensed social worker and a AYA cancer survivor herself who underwent a bone marrow transplant in her 20s as well. And then we recently received funding from a wonderful organization, the Lions Foundation, to hire an AYA psychologist. So a psychologist who will specifically see every single one of our AYA patients with cancer and be able to provide services both in the hospital and outside of the hospital.

And then we also have a great dedicated nursing team who will see all of these patients and make sure that they're getting the care that they need.

It's a huge multidisciplinary team. And probably the most important is actually a pharmacist who's in our clinic every week, too, because these AYA protocols take a lot of medication monitoring, a lot of adjustment and are really complicated. And having the pharmacist there to do that is incredibly important.

And we also have a genetic counselor who will see our patients that we think are high risk for genetic diseases that predispose them to their cancer, so really a holistic approach to the patients. There's no requirements to call yourself an AYA program, there's no right way of doing it. It's whatever resources you can kind of cobble together. These aren't resources that are reimbursed by insurances. As you can tell

just by what I said, we require a lot of philanthropy, we require a lot of extra help outside of programs because these things don't get paid for by the traditional medical system. But they're so sorely needed that it's left to wonderful people like Dr. Stock and others throughout the country to kind of beg, borrow, and steal the resources they need for all these different patients.

And then I started a program here where we'll see any young patient with cancer, so whether you have ovarian cancer or colon cancer or whatever cancer there is. Basically, I'd be willing to see you and I specialize in sexual health and fertility and we'll talk to them about those topics specifically but they'll also need our program administrator who's connected to a lot of community and national resources, our psychologists to get in touch with them and really help kind of shepherd them through their cancer experience and provide the extra support that you're not going to get in the traditional oncology office.

Lizette: That's great.

Elissa: Love to hear about this whole comprehensive approach to young adult care. That's wonderful.

Lizette: Yeah. It's great that you're treating the whole person. I love that.

Dr. DuVall: Yeah. That's what we try to do and that's what most of the research I focus on is actually trying to do. The same clinical trials that we do to improve survival, improve outcomes and to actually use those clinical trials to look at interventions that can improve our psychosocial outcomes as well.

And this is something that is happening in our clinical trials in general. We're including health-related quality of life measures and patient-reported outcome measures in trials because even if we do have equivalent survival outcomes, if people are living the same amount after, on either try that we do but say, the neuropathy or the fatigue or the chemo brain or what have you, you could list any number of things that every

person whose gone through cancer can easily identify with. If those are better on a different arm, then we should probably be using that treatment instead of the standard if it is better. Even though the survival isn't different, if we're still decreasing the burden to our patients, that's what we should be doing.

That's where the field is moving also and it's very exciting and it's kind of where I'm trying to be more active in that.

Elissa: Absolutely. And when you're doing clinical trials as well, I mean that can have an impact, really, all over the country, all over the world. I know there are some other young adult programs at major centers around the country, but there could certainly be more, and so I hope that the clinical trials will show what a benefit they are to young adult patients and major cancer centers can start putting together some more programs to help because I love to hear about this comprehensive approach. I think that sounds just amazing.

Now I'd like to finish up today with a question for you. On our patient podcast home page, we have a quote that says, "After diagnosis comes hope." What would each of you say to patients and their families to provide them hope for the future?

Dr. Liu: Yeah. I think, compared to the decades ago, we made a huge progress in the treatment of leukemia, and forgot to mention even, for the patient, with the very complex acute leukemia when we have a comprehensive clinic, they call that Complex Acute Leukemia and Myeloid Malignancy Clinic, they call that CALMM clinic. We have leukemia physicians, also transplant physicians working together and now provide all the up-to-date clinical trials and to the patient to treat them than take them to the transplant, provide a cure.

I think right now there's a higher hope to be cured. I always tell my patient, and I know that especially for the young AML patient, the goal of treatment is cure, right, either cure with chemotherapy or cure through the standard therapy and the stem cell transplant. That's my goal.

Now for the older patients we can also help to control the disease to preserve a quality of life. That's a difficult, but we can always help as a physician with a new development, new treatment options.

Dr. DuVall: I always tell my patients that I'm a realistic optimist. I think that we always need to talk about what's actually going on and talk about the reality of the situation, but there is absolutely no reason to have not a ton of hope, and there's no reason not to be very optimistic about what's happening. And a lot of that is because of the available therapies that we have that are currently now available that never were even 5, 10, 15 years ago and the hope for the future of, even having more of them.

There's lots of development that's going on. There's lots of availability of different approaches that are really trying to take into account the more and more nuanced genetic markers that we're seeing that we're learning about, and that potentially will have just as much impact as what some of the big breakthroughs have over the last 10 years. So there's lots and lots of hope out there for any patient with a blood cancer at this point.

We still have a ways to go. We're still not at 100% cure, and that is the goal. So, there is still not a perfect science out there, but with what we have available, we can do a lot of good, and we can do it pretty well for most people.

Elissa: That's wonderful. Well thank you so very much, Dr. Liu, Dr. DuVall, for joining us today. It was really exciting to hear just about all the different kinds of cellular therapies that are out there that, hopefully, we'll get to a point where we are providing a cure for acute leukemias. And thank you for telling us about these comprehensive programs, like the AYA program and the CALMM clinic. It's such a good thing to have to really look at that comprehensive approach, that holistic approach to the patient. We love hearing about it, and we hope that that will be good models for the future at all the major cancer centers.

So thank you both so very much for being here with us today.

Dr. Liu: Thank you very much.

Dr. DuVall: Yeah. Thank you so much for having us. It was a pleasure.

Elissa: Also, a special thank you to University of Chicago Medicine for supporting this episode. 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 can be found in the Show Notes or at TheBloodline.org. This is your opportunity to provide feedback and suggested topics that will help so many people. We would also like to know about you and how we can serve you better. The survey is completely anonymous and no identifying information will be taken. 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 find more information about acute leukemias at LLS.org/Leukemia or CAR T-cell therapy at LLS.org/CARTTherapy. All of these links, including information about the programs that University of Chicago Medicine offers, will be in the Show Notes or at TheBloodLine.org.

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