

THE BLOODLINE WITH LLS

A PODCAST FOR PATIENTS AND CAREGIVERS

Episode: 'Tackling Lymphoma: Recent Advances in Immunotherapy'

Description:

Join us as we report on the latest developments in immunotherapy from the 62nd American Society of Hematology (ASH) Annual Meeting and Exposition that was hosted virtually December 5-8, 2020. In this episode, we will be speaking to Dr. Laurie Sehn, a Clinical Professor and Researcher with the British Columbia Cancer Centre for Lymphoid Cancer and The University of British Columbia. Immunotherapy was a primary topic at this year's ASH meeting. Dr. Sehn shares exciting news about the advancements in immunotherapy for Non-Hodgkin Lymphoma. Hear why lymphoma is a great candidate for immunotherapy, how it works, and how a collaboration of researchers from around the world is accelerating the number of new and effective treatments available for lymphoma patients.

Transcript:

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

Edith: I'm Edith.

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

Elissa: Each year the American Society of Hematology or ASH hosts a Meeting and Exposition to present on the latest advances in research on blood cancers and diseases. Physicians and researchers from around the world attend the conference to share their research and discoveries. As with all events in 2020, the 62nd Annual ASH meeting was moved to a virtual format; and it was held December 5-8.

One of the primary topics was immunotherapy. We wanted our listeners to hear about the exciting advances in the use of immunotherapies on non-Hodgkin lymphomas. Today we'll be speaking to one of those researchers who presented at ASH, Dr. Laurie Sehn. Welcome Dr. Sehn.

Dr. Sehn: Thank you, it's my pleasure to be here today.

Elissa: So, tell us a little bit about the ASH conference. What was it like in the virtual setting?

Dr. Sehn: Well, you know, I'd have to say that ASH is by far the most important meeting of the year for hematologists and hematology/oncologists. So, in a normal year, it takes place in person and I would say that probably now more than 30,000 attendees are present. So, it's usually a really bustling event and allows opportunity for networking and a lot of information exchanged. So, this, of course was a very unique year whereas along with many other meetings was forced to go virtual.

But I have to say that I think it far surpassed everybody's expectations, and maybe because there's been a big lead-up to this meeting where other meetings have tested the waters and they chose to kind of modify the format based on what seems to have been working in other meetings. But I'd say that it was done extremely well, where there was a combination of prerecorded lectures as well as interactive forums and there was opportunity for question-and-answer periods. And, in my impression, it all seemed to go quite smoothly.

Elissa: Oh, that's great.

Edith: So, doctor, what are you most excited about from this year's ASH meeting?

Dr. Sehn: So, you know, I'm a lymphoma researcher, both a clinician and clinical investigator, so I pay most of my attention to what's going on in the world of lymphoma. And there certainly is a huge amount to be excited about.

This year, what we've seen for I would say the last decade is just a continuous development of novel therapies for lymphoma. I think that for years and years we were relying solely on chemotherapy as the mainstay of treatment for lymphomas. And it took a while for the therapy to catch up with the biology; but, due to advances

in biological understanding of lymphoma, and lymphoma, of course, is not one thing. It's many different types of cancer of lymphoid cells. And we've seen advances in our biological understanding over the last two decades that clearly have translated into novel therapies. And, by far, the most exciting novel therapy or group of therapies has been immunotherapy.

Lizette: And, doctor, why are lymphomas such a good candidate for immunotherapy?

Dr. Sehn: So lymphoid cancer and lymphomas, by definition, are immune cancers. So, we know that they exist surrounded by the immune system. So, most lymphomas grow in the immune structures of our body, meaning lymph nodes and spleen and bone marrow and they're intimately associated with the normal cells in the immune system. And I think, we also understand that the immune system is important, probably not only for continuously fighting off lymphoma within our own body, but also for possibly sort of sustaining it in some respect. So, there's this give and take between lymphoma and the immune system. I think that continuously happens.

So, it's really primed for immunotherapy in that there's probably always this communication between lymphoma and the body's immune cells; and what immunotherapy aims to do is to try and control that communication and to try and direct the communication in such a way that the immune cells are actually getting an advantage and basically overtaking the lymphoma cells.

Lizette: And you mention that there's several types of lymphomas. What types of lymphomas are really benefitting from immunotherapy?

Dr. Sehn: Well, that's the fascinating thing, that we're seeing benefit across the spectrum of lymphomas. So, the classification of lymphomas, really a complicated list at this point. The WHO classification or World Health Organization classification lists more than 50 different types of lymphomas, depending on how you count them.

As patients and clinicians, we often divide them into categories based on behavior. So, we might refer to some of them as aggressive lymphoma based on those that grow more rapidly or indolent lymphoma, based on those that grow more slowly. But across the board we're seeing immunotherapies that are having benefit in both indolent and aggressive lymphomas.

Lizette: Wow, that's really great.

Elissa: In your studies, why did you choose to focus on lymphoma?

Dr. Sehn: So, you know, again, my primary role is a lymphoma researcher; and the immunotherapy studies that are emerging are particularly exciting in this area. Certainly, for my colleagues that do solid tumors, we're seeing progress in that vein as well. But focusing on lymphoma today, I'd say that advances are clearly being made where these therapies are emerging and becoming reality and available for patients.

Elissa: That's great. The ASH meeting seems to show a lot of really good collaboration amongst different countries. You're joining us from British Columbia, Canada, and how do you feel about the recent advances in immunotherapy from researchers just around the world?

Dr. Sehn: Well, that is really the advantage of having a large international meeting. It brings everybody together in the same place. And this time it was at the same virtual spot. But it provides an opportunity for people to share their research from around the world.

Importantly, and I think everybody probably understands this already is that, you know, most of the research being done is done in a collaborative, international way already. So as therapies advance through clinical trials, they usually go from perhaps small local trials very quickly to international collaborations because everybody's goal is to, number one, get patients around the world access to novel therapies as they're in development but also to speed up the clinical development of many of these promising

new therapies so that we can make advances quicker; and that really requires usually international collaboration.

So many of the studies that are presented at a meeting like ASH are presented by investigators from around the world. But there's a very good chance that the information they're presenting is actually based on a clinical trial, for example, that's been done, across the world itself in an international multicenter setting.

Elissa: I'm sure a lot of our listeners today just have no idea how much collaboration there is internationally; and I'm sure they think that, you know, doctors over in Europe are doing one thing and US doctors are doing another thing, Canadian researchers are doing another thing, and so it's really good to hear just how much collaboration goes into this because as the end of the day we all want to end cancer.

Dr. Sehn: Absolutely! So that collaboration goes on at every level of development. So right through from basic science to the multicenter Phase III trials or randomized trials that are usually required to bring new products and, and new exciting therapies into the market essentially.

Elissa: So, from the various studies that you saw presented and what you presented yourself, was there a few things that you were particularly excited about?

Dr. Sehn: Yes, so we've been talking about immunotherapy; and, of course, immunotherapy is a broad term that really refers to therapies that are designed to harness the activity of the immune system to fight off cancers, and in this case, we're talking about lymphoma cells.

I'd say that the two areas that we're seeing really the most remarkable advances are in, first of all, CAR T-cell therapy. People have heard about CAR T-cell therapy for a while because it's a treatment that is now available in some countries to treat people with lymphoma. But CAR T-cell therapy is essentially a gene-modified cellular therapy which, in terms of the CAR T-cell therapy that is currently available in the clinical

setting, usually refers to patients' own cells that are actually filtered out and then modified genetically and then given back to the same patient to fight off their cancer in a very directed way.

And we saw studies on CAR T-cell therapy emerge several years ago, leading to the development of CAR T-cell therapy as an actual treatment. But there are continuing ongoing trials in CAR T-cell therapy that are basically showing us that in addition to the original patients that benefitted, which was primarily patients with aggressive B-cell lymphomas, we're now seeing benefit in other types of lymphoma like mantle cell lymphoma, follicular lymphoma, multiple myeloma. So really an expansion of indications are being explored with some very exciting results and looking very promising.

In addition to that kind of CAR T-cell therapy that we're seeing explored in other settings than it was originally made available for, we're also seeing new types of CAR T-cells being developed. So, the current kind of CAR T-cell therapy, as you can imagine is quite effortful, so it requires taking cells out of one person, genetically modifying them, giving them back to that same person. So, it's a very almost designer-based treatment.

And the goal in the future probably is to develop CAR T-cell therapies that are a little bit more broadly available, so where you can have cells available. So there might be a donor cell that is used to make CAR T-cells that then can be used for multiple people so you don't have to rely on that, patients' own T-cells but you're getting these donors' T-cells that are made as a product, so they're often being referred to as off-the-shelf CAR T-cells so you don't have to make them for the individual person, but basically you've got this closet full of CAR T-cells that have been made and are ready to go so they could really speed up the timeline of getting people the CAR T-cell therapy rather than kind of the slower timeline with the original process. And we did see more data coming out on these so-called off-the-shelf CAR T-cell, which I think was very exciting.

Elissa: That's amazing. Wow! Yeah, I mean, we're really excited to just see what happens with all that. I mean if we could have that CAR T-cell therapy just so readily available for so many patients, that would just be incredible.

Dr. Sehn: Correct. So that's a major development that is in the works, and I think we saw some exciting data on that.

The other change in CAR T is that we know that the original CAR T-cells had a particular target that they were designed to aim at. And we now have CAR T products in the works that are exploring using other targets or sometimes, more than one target, so you can have a CAR T-cell that's designed not only to target CD19 as, for example, the current CAR T-cells that are on the market are currently targeting, but you can target CD19 and another marker that, you know, maybe together by targeting two things at once, you could see more benefit. Or if CAR T-cells targeting CD-19 don't work, maybe you can move to a different CAR T-cell that has a different target that it's exploiting. So, there's really been an expansion of CAR T-cells looking at basically exploiting other molecules that are in lymphoma cells that perhaps we can direct the CAR T-cells against.

Elissa: And just so our listeners understand, with CAR T therapy, we're really trying to have it track down the bad cells. Have it track down those cancer cells and leave the healthy cells alone, correct? So, they're looking for something in particular on those cancer cells.

Dr. Sehn: That is correct. So, CAR T-cells have been really engineered to find a marker that is present on lymphoma cells. Unfortunately, you know, the marker that's currently being utilized, CD19, is excellent in some ways because it's present on most B-cell lymphomas, but it's not selective for B-cell lymphoma. So, you know, part of the side product of CAR T is that it does affect some of the normal B-cells in the body, but, importantly, those recover. So, it is responsible for some of the side effects of CAR T, but it doesn't stop them from being beneficial.

Elissa: So, with the CAR T therapies, are we using these as frontline treatments for lymphomas? So, the first treatment that they get or are they more used for after their relapse?

Dr. Sehn: So originally the CAR T-cell that has been approved and is on the market for treatment was approved for patients who had received at least two lines of therapy, so essentially relapsed disease, although we are seeing data now looking at the use of CAR T-cells earlier on. So, we saw some data presented at ASH where they're looking at patients who had had only one prior line of therapy and also, very exciting, we ha-, we saw at least one trial that looked at patients who had not had any chemotherapy. So-

Elissa: Wow!

Dr. Sehn: -this particular study took a group of patients with aggressive B-cell lymphoma who normally would be potentially treated with fairly aggressive chemotherapy, but we know that that's not suitable for all patients. So, they took a group of patients who were felt to be not suitable for chemotherapy but would have had probably more limited treatment options and tried CAR T-cells in that setting. And, and we saw remarkably high response rates. And the data is still relatively early, but some of those patients had a complete response and are remaining in complete response with months of follow-up. So, I think that's very exciting because we're now starting to see attempts to see whether or not we can replace chemotherapy with CAR T-cells in some setting. So that certainly is a very exciting area of research.

Elissa: Yes, definitely.

Lizette: We get that question all the time from our patients, whether it's being studied in frontline, or can they speed up the research because they're really wanting some type of treatment that they say is less toxic. And to them it really means not having as many long-term or late effects or side effects.

Dr. Sehn: Absolutely. I mean I think we all have the same goal, and that is to minimize side effects while finding effective treatments for lymphoma. And, you know, I think if we can eventually replace chemotherapy with immune therapies, such as CAR T-cell therapy, I think that would be real progress.

Elissa: So many of our listeners today could either be lymphoma patients or have a loved one with lymphoma. What would you say to these patients and caregivers now about the potential future of immunotherapy treatments and how they can remain hopeful?

Dr. Sehn: I would say that it's a very exciting time for advances in lymphoma treatment. I personally, you know, often tell my patients that there are many treatments coming through development. We used to say, "Oh, in the future, we're hoping for advances and research will bring new things, hopefully." But research is bringing the coming new therapy options. Yes, and not only coming; to a certain extent, many things are here already, but other things are coming in real time where I have no doubt, they will be practically available for many patients out there who may not need treatment today but are thinking what's my next step? And, and the reality is things are changing very quickly and new treatments are emerging in real time.

So, I think it's important for patients and families to at every part in their therapy when there's a decision to be made perhaps as to what therapy might be the next best therapy for them or what choices they should make is to be aware of all of the options. And, those options may include some therapies that are newly becoming available or they may include clinical trials of some therapies that are not yet available but are showing a lot of promise that they could potentially get access to.

So, having a good open relationship with your medical oncologist and make sure that you're staying abreast with, you know, everything that's going on in terms of development I think is important. Of course, that's your medical oncologist's job, but I think-

Elissa: Yes.

Dr. Sehn: - having that conversation at each point saying, "You know, what are the options here? What should I be thinking about? You know, what perhaps can I also be thinking about in terms of clinical trials?"

Elissa: It's good to stay informed, definitely.

Dr. Sehn: Absolutely.

Elissa: And that is just so exciting. I'm really excited to hear about all the advances that were talked about at ASH just coming from around the world. And we thank you so much, Dr. Sehn, for joining us today and sharing your expertise and experience with us and our listeners.

Dr. Sehn: It has been my absolute pleasure. Thank you for the invitation.

Edith: Thank you.

Lizette: Thank you so much.

Elissa: And thank you to everyone listening today. *The Bloodline with LLS* is one part of the mission of The Leukemia & Lymphoma Society to improve the 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.

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