

## WELCOME AND INTRODUCTION

### **Operator**

Greetings, and welcome to the Update on Peripheral T-cell Lymphoma (PTCL) telephone and Web education program. It is now my pleasure to introduce your moderator, Lizette Figueroa.

### **[Slide 1 – Welcome and Introductions]**

### **Lizette Figueroa**

Thank you. Hello, everyone. On behalf of The Leukemia & Lymphoma Society (LLS), a warm welcome to all of you. Special thanks to Dr. Lauren Pinter-Brown for sharing her time and expertise with us today. We have over 500 people participating from across the United States and several countries around the world, including Canada, Guatemala, Thailand, the United Kingdom, and Venezuela.

For more than 60 years, The Leukemia & Lymphoma Society has helped pioneer innovations such as targeted therapies and immunotherapies that have improved survival rates and quality of life for many blood cancer patients. To date, we have invested more than one billion dollars in research to advance therapies and save lives. Until there is a cure, The Leukemia & Lymphoma Society will continue to fund promising research from bench to bedside. We would like to acknowledge and thank Celgene Corporation for support of this program.

### **[Slide 2 – Lauren C. Pinter-Brown, MD, FACP]**

I am now pleased to introduce Dr. Lauren Pinter-Brown, Clinical Professor of Medicine at the David Geffen School of Medicine at the University of California (UCLA) in Los Angeles, California. On behalf of The Leukemia & Lymphoma Society, thank you so much for volunteering your time and expertise.

Dr. Pinter-Brown, I'm now privileged to turn the program over to you.

## PRESENTATION

### **[Slide 3 – Disclosures]**

### **Lauren C. Pinter-Brown, MD, FACP**

Thank you so much. And thank you all for joining us this morning and for your interest in T-cell lymphomas.

### **[Slide 4 – T-cell Lymphomas]**

As is shown on this slide, T-cell lymphomas account for only 15% of all the non-Hodgkin lymphomas in the US. The majority of non-Hodgkin lymphomas in the US are B-cell lymphomas. But just like B-cell lymphomas, there are many different kinds of T-cell lymphomas that are quite different in the way that they present and the way that the pathologist sees the slides, in their behavior and in their outlook. Interpretation of the pathologic material may be quite difficult for a general pathologist and, obviously, this is so important to ensure the appropriate management of a patient that we have exactly the accurate diagnosis.

## **Dr. Pinter-Brown**

Part of the issue is that as we learn more and more about T-cell lymphomas, the classifications and the different subtypes that are recognized are changing, and so someone that doesn't come into contact with this frequently may have difficulty keeping up with all the different changes as knowledge increases. The other difficulty in the therapy of patients with T-cell lymphoma is that there is no standard therapy at this time. The treatments that work well for B-cell lymphomas do not always work well in the treatment of T-cell lymphomas, underscoring the need that we have for having novel therapies for T-cell lymphomas in this patient population.

### **[Slide 5 – Classification of PTCL]**

The current classification of peripheral T-cell lymphoma is listed here, and you'll see that it's a little complex. And I'm going to go through it in some detail because it's very, very important to understand. In the new World Health Organization (WHO) classification, I think peripheral T-cell lymphoma will now be classified as mature T-cell lymphoma. That will help everyone, I think, understand a little bit more what conditions we're speaking about because there's a lot of confusion about what peripheral means. Does it mean that you have lymph nodes? You know, what exactly does it mean?

But, truly, what people are talking about when they're talking about peripheral T-cell lymphomas are T-cell lymphomas that come from mature T cells. So that's different from the precursor lymphoid neoplasms that you see here on the left in the kind of buff-colored box. Those are cells that are very immature and basically can be called T-acute lymphoblastic leukemia/lymphoma. They're very different from the diseases we're talking about now.

So focusing on the right side of the slide, the mature T-cell neoplasms, we see that one way of understanding all these different kinds is to focus on the tissue where they usually present or show up to a patient or a doctor. So there are lymphomas that are cutaneous or skin primary lymphomas. There are some that are extranodal—that means they're not in a lymph node. They can be in the nose, they can be in the intestines, they can be in the liver, and they can be in the fat of the skin. There are nodal lymphomas, those that truly begin and show up in lymph nodes. And then there are some that are leukemic or show up in the blood, the most common being adult T-cell leukemia/lymphoma (ATLL).

Additionally, on this slide, you'll see that these boxes, if you will, are color coded. So, red means that the behavior is somewhat aggressive or fast growing, and buff means that it's indolent. So, in general, what you see here is that the cutaneous T-cell lymphomas, in large part, are indolent lymphomas and the other presentations are much more aggressive.

### **[Slide 6 – Classification of PTCL (cont.)]**

Again, kind of so that you can see this a little bit better, we have extranodal lymphomas, nodal lymphomas, and leukemic lymphomas; and here the color code yellow is indolent.

### **[Slide 7 – Classification of PTCL (cont.)]**

And then we have the primary skin lymphomas, the first three in black being the primarily indolent T-cell lymphomas of the skin.

## [Slide 8 – Common Peripheral T-cell Lymphoma Subtypes (excluding CTCLs)]

### **Dr. Pinter-Brown**

So if we're talking about common peripheral T-cell lymphoma subtypes, this is in the US, the three most common kinds are peripheral T-cell lymphoma—it's NOS, not otherwise specified—angiimmunoblastic lymphoma (AILT), and anaplastic large-cell lymphoma (ALCL). It speaks a lot towards our lack of knowledge about T-cell lymphomas that one of the most common subtypes is something called peripheral T-cell lymphoma-not otherwise specified. What that means to the pathologist is that this particular lymphoma is a T-cell lymphoma. It doesn't nicely fit into the boxes and so it's kind of a garbage bag, if you want, of a lot of different lymphomas that don't clearly fit a description of any of these other named lymphomas. And that tells us a lot about our lack of knowledge about all the different kinds of peripheral T-cell lymphomas.

## [Slide 9 – PTCL Epidemiology]

Peripheral T-cell lymphoma subtypes and T-cell lymphoma's incidence very much differs by geography in the world, so that we see that peripheral T-cell lymphoma-not otherwise specified, the garbage pail here, is the same across the world, but certain kinds of T-cell lymphomas are much more common, for instance, in other countries. Natural killer (NK) T-cell lymphoma or adult T-cell leukemia/lymphoma are much more common in Asian countries. So, that highlights the need for an international community to really come together and learn about these lymphomas because, in some countries, there may not be as much expertise because there is not as much experience with T-cell lymphomas in general or with specific T-cell lymphoma subtypes.

## [Slide 10 – Diagnostic Workup of a Patient]

So, as I mentioned before, the hallmark of treating any patient with lymphoma is the diagnosis. If we get the wrong diagnosis, we go down the wrong path; we may use a treatment that's not effective enough. And so in T-cell lymphomas, it happens to be very important that the pathologist even hear about the history and physical examination, and maybe even some of the laboratory testing that's done for a patient, and to be able to arrive at an accurate diagnosis. And this is true even more so for T-cell lymphomas than for B-cell lymphomas. This following information then leads the pathologist to a diagnosis, and this guides further testing and staging for the patients.

One thing that's really important to note is there is test called T-cell gene rearrangement. It's a very, very sensitive test that shows people, hopefully when it's working, that there is a clone of T cells—and that's the hallmark of any lymphoma, that it's a clone of cells. Unfortunately, and there is a lot of misunderstanding about this, T-cell gene rearrangement positivity, or the finding of this, does not actually make the diagnosis of T-cell lymphoma. So, the pathologist here needs to see with their eyes a slide that looks like T-cell lymphoma and fits the characteristics, not just a T-cell gene rearrangement. And that's a very common misconception, particularly in the community.

## [Slide 11 – Diagnosis of PTCL]

So, when the pathologist is making a diagnosis of any peripheral T-cell lymphoma, they use what's called immunohistochemical stains. These are examples. They always, if it's positive, turn brown. Some people call it brown pathology. It's very important to know that approximately 10% of peripheral T-cell lymphoma cases are incorrectly diagnosed, particularly in the community. Again, it's because these are not very commonly seen. The subtyping is always changing. So it may be particularly

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important for someone to get a second pathologic opinion by an expert in this area. And there are pathologists that focus on T-cell lymphoma, just as there are oncologists that do the same.

So there are a lot of different stains here. There are some that are fairly unique to T cells—cluster of differentiation, CD3, CD2, CD5, CD4, and CD8 tell us that it's a helper or a suppressor T cell. And then we see some stains that happen both in T cells and B cells.

So we see CD20, which is the hallmark of B-cell lymphomas and B cells that are normal, but occasionally T-cell lymphomas will also have CD20.

CD10 is a stain for follicular lymphoma, that's a B-cell lymphoma; but there's a certain T-cell lymphoma that also has this stain, angioimmunoblastic T-cell lymphoma.

And then we see CD30 that's an activation marker. It happens both in B- and T-cell lymphomas in some normal tissues, and it's become particularly important because we now have a treatment modality that targets cells that express CD30 on their surface.

## **[Slide 12 – NCCN Guidelines for Initial Treatment of PTCL]**

National Comprehensive Cancer Network (NCCN) is a group of comprehensive cancer centers that gets together and comes to a consensus or agreement within the committee about guidelines for treatment, for evaluation of patients. I show here [on slide 12] the NCCN guidelines for the initial treatment of peripheral T-cell lymphomas. These are primarily the lymphomas that are not cutaneous lymphomas and there are separate guidelines for that. While every doctor may not exactly agree with all these guidelines, they are stated in such a wide manner as to allow patients and physicians who don't have a lot of experience with these disorders to get some guidance about what might be appropriate therapies.

So, in these particular disorders, something very interesting has occurred, and that is that the NCCN suggests that clinical trials are the preferred method of treating a patient. That is because our knowledge of T-cell lymphomas lag so far behind B-cell lymphomas, and the only way we're going to learn what the appropriate treatment is, is to perform clinical trials. And I'll be talking a little bit more about the trials that are open at this time. Additionally, there is no standard therapy, so a clinical trial may offer a better therapy than what an oncologist might pick.

There are a whole host of suggested regimens here—some based on medical knowledge, some based on the opinion of the people in the committees. We notice that for other subtypes, not anaplastic lymphoma kinase (ALK)-positive anaplastic large-cell lymphoma that, upon achievement of complete remission (CR), that a consideration for consolidation with high-dose therapy with stem cell rescue is listed there. And that is because, unfortunately, with the current treatments that we have, many patients with peripheral T-cell lymphoma will relapse. And we hope that with consolidation with high-dose therapy, we can prolong their remissions and effect a higher chance of cure.

Now ALK-positive anaplastic large-cell lymphoma is listed separately here. They list two induction therapies, CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone), just like is used for B-cell lymphomas without the Rituxan® (rituximab) or CHOEP, which is CHOP with a drug called

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etoposide, hence the E. And for these patients, if they attain a complete remission, that high-dose therapy with autologous stem cell rescue is not recommended.

### **[Slide 13 – NCCN Treatment Guidelines for Relapsed/Refractory PTCL]**

There are also NCCN treatment guidelines for relapsed and refractory peripheral T-cell lymphoma. Again, you'll see that these patients have been divided into whether they are candidates for transplantation or not. You'll also see that even in both columns, the clinical trial participation is preferred rather than some of these suggestions that are here. And you see that there's a very long list of possible choices of treatments. Again, some of them are very well studied, some of them not so well studied. You'll even see, which is unique to this kind of lymphoma, in the candidates for transplantation at the bottom, two drugs being suggested with use by themselves without a combination such as all the other drugs that are up on top [of slide 13]. And that's because these drugs have been studied extremely well and people are confident about what the response rates are.

### **[Slide 14 – Relapsed/Refractory PTCL: FDA-Approved Agents]**

There are currently three U.S. Food and Drug Administration (FDA)-approved agents for relapsed and refractory peripheral T-cell lymphoma. One of them is called romidepsin (Istodax®). It is a histone deacetylase (HDAC) inhibitor. I'll explain that a little bit in the coming slides. The other is pralatrexate (Folotyn®). It is a drug that's kind of a designer methotrexate (Trexall®, Rheumatrex®), which is an old chemotherapeutic agent. And then there's brentuximab vedotin (Adcetris®), which is FDA approved specifically for anaplastic large-cell lymphoma. And this is an antibody drug conjugate. That means it's an antibody that seeks out cells that have CD30 on their surface and it has been tied to a single chemotherapeutic agent called auristatin. And the auristatin then gets into these cells and actually kills the cells. You'll see here [on slide 14] the *N* means how many patients were studied to allow the FDA approval and CR means complete response rate and response duration, how long these responses lasted in these pivotal trials that allowed FDA approval of these agents.

### **[Slide 15 – Pralatrexate]**

So, I'm going to talk about these agents separately because they represent unique agents for T-cell lymphoma. As I mentioned before, this is something that really is desperately needed. So pralatrexate is a more kind of chemotherapeutic drug. This cartoon shows you a cancer cell and shows you that the drug gets in through something called reduced folate carrier-1 (RFC-1) and then gets into the cell and stays into the cell much longer than methotrexate because of the way that it is metabolized. And then it actually uses the same enzyme to kill the cell, an enzyme which it inhibits.

### **[Slide 16 – HDAC Inhibitors in MF/SS]**

HDAC inhibitors were first studied in mycosis fungoides and Sézary syndrome. Those are primary cutaneous T-cell lymphomas and there are two of them that are FDA approved—one is called vorinostat (Zolinza®), the other as I mentioned romidepsin. Vorinostat is a pill. Romidepsin is an intravenous drug. But romidepsin has been studied both in cutaneous T-cell lymphoma and in peripheral T-cell lymphoma, the nodal kind, and is FDA approved for both, whereas vorinostat was studied only for cutaneous T-cell lymphomas. And you'll see their side effects are very, very similar. Primarily fatigue, some anorexia, which means that you don't feel like eating and that the food tastes funny, and some laboratory abnormalities. And these are things that can be managed but are

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different from the side effects from pralatrexate, more of a chemotherapeutic agent where you see mouth sores primarily as a side effect in that drug.

### **[Slide 17 – Histone Deacetylation Results in Transcriptional Repression]**

How do histone deacetylase inhibitors work? And this is kind of a complicated thing. But in our cells' genetic apparatus, we have deoxyribonucleic acid (DNA), and there's lots of it. And it's organized by wrapping it around these things called nucleosomes. Those are the green kind of rectangular boxes, kind of like thread is wrapped around a spindle. And you can either unwrap the DNA or wrap it up close to the histones depending on how much of the genes you want to be seen and transcribed. So what histone deacetylase inhibitors do is allow the opening of the DNA so that more genes can be transcribed. And the transcription of these genes lead to the cancer cell's death.

### **[Slide 18 – Brentuximab Vedotin (SGN-35): Antibody-Drug Conjugate]**

Brentuximab vedotin, as I mentioned, is an antibody drug conjugate. You see it as a little Y here [on slide 18] in this cartoon in the left upper corner. It attaches to a cell that has CD30 on its surface and then it gets into the cell. The chemotherapeutic agent detaches and then kills the cell by being a tubulin poison. The tubulins, you'll see here, they look a little bit like hands with fingers maybe pulling apart, and they're the things that help the cell divide into two cells. So when they're poisoned, the cell can't divide any longer.

### **[Slide 19 – Ongoing Phase III Trials: PTCL]**

I said I would talk about ongoing phase III trials in peripheral T-cell lymphoma. Phase III trials means that there are two things being compared, the standard arm, if you will, something that people would use routinely and then the experimental arm. And it's relatively recent that phase III trials have been ongoing in peripheral T-cell lymphomas or in cutaneous T-cell lymphomas because of the rarity of these conditions and the fact that they're spread all over the world. But, thankfully, more recently with the Internet and all kinds of technological advances, people from all over the world can do studies together. And so these trials represent those efforts, people from lots of different countries doing trials.

The first is alemtuzumab (Campath®), which is an antibody against CD52 plus CHOP. The second is alisertib (MLN8237)—I'll go through that a little bit, which is aurora kinase inhibitor versus what we have now approved in the US, pralatrexate or romidepsin. And gemcitabine (Gemzar®) was added because there are sites that are not in the United States. Brentuximab vedotin versus CHP (cyclophosphamide, doxorubicin, prednisone)—that's CHOP without the vincristine—because brentuximab vedotin causes a neuropathy like vincristine, so the drugs can't be added together in the same regimen. And these are for CD30-positive peripheral T-cell lymphomas. Another study looking at CHOP to get someone into a complete or partial remission and then using pralatrexate as a maintenance. The addition of romidepsin to CHOP versus CHOP. And, finally, heliostat, which is another HDAC inhibitor plus CHOP versus CHOP, which will be opening soon. So these are all ongoing trials and you see in the left lower corner their numbers if you went to [clinicaltrials.gov](http://clinicaltrials.gov) and wanted to look up what their eligibility or goals were.

## [Slide 20 – Ongoing Phase III Trials: CTCL]

### **Dr. Pinter-Brown**

In cutaneous T-cell lymphomas, there are two phase III trials going on. One is brentuximab vedotin versus investigator's choice, which is methotrexate or bexarotene (Targretin®), a retinoid, like a vitamin A-related drug for patients who have CD30-positive cutaneous T-cell lymphomas. And another trial with a drug called KW-0761 (mogamulizumab) versus vorinostat, again, for relapsed and refractory cutaneous T-cell lymphoma. KW-0761 is an antibody against something called C-C chemokine receptor (CCR)4. I'm going to go into a little bit. If any of you know about B-cell lymphomas, you know that an antibody, rituximab, was a breakthrough drug in the treatment of B-cell lymphomas. And we continue to look for our antibody for those of us that are particularly focused on T-cell lymphomas.

## [Slide 21 – Alisertib: Kinase Inhibitor]

As I mentioned, alisertib is an aurora kinase inhibitor. It's a pill and it kills the cell by regulating mitotic signaling. Mitosis is the process with which cells are divided.

## [Slide 22 – Mogamulizumab (KW-0761): Anti-CCR4 Monoclonal Antibody]

And mogamulizumab, or KW-0761, is an antibody. It is against CCR4 that is on the cell surface and has already been approved in Japan for the treatment of adult T-cell leukemia and lymphoma, which is a condition endemic to Japan but seen in other places of the world, that has been relatively chemoinensitive. So it was very exciting that this antibody not only worked in this patient population but was well tolerated. And studies are ongoing in other parts of the world for other T-cell lymphomas.

## [Slide 23 – Drugs to watch out for]

Drugs to watch out for, phosphoinositide PI3-kinase inhibitors are drugs that have received a tremendous amount of press for B-cell lymphomas. They affect a pathway that's called the B-cell receptor signaling pathway, but we're learning that maybe this is a pathway that's common to many cells, not just B cells. So some of the drugs that are now being looked at in B-cell lymphomas may be drugs that we want to look at in T-cell lymphomas.

Additionally, there are programmed cell death PD-1 inhibitors. These are drugs currently that are being used on what's called solid tumors, melanomas, lung cancer, but definitely will have a role in lymphoma and, specifically, in T-cell lymphomas.

And then there are dual PI3-kinase inhibitors that are being studied. Again, things that target this B-cell receptor signaling pathway but may actually be useful for T-cell lymphomas, too.

## [Slide 24 – How might we treat in the future? How are we treating now?]

So, how might we treat in the future? How are we treating now? Increasing attention should be paid to whether the lymphoma is a T-cell lymphoma or a B-cell lymphoma because the treatments are not always going to be the same now. Increasing attention should be paid to the subtype of T-cell lymphomas. So, I've listed here their acronyms, and I apologize for that but, really, the idea is that there are specific subtypes of peripheral T-cell lymphoma that have specific treatments that are useful in that patient population. So, at this point, it's really not okay for us to say somebody has a peripheral

**Dr. Pinter-Brown**

T-cell lymphoma. We have to understand the subtype so that we can guide therapy much more accurately.

**[Slide 25 – Functional Subsets of PTCL]**

One suggestion made at a recent lymphoma workshop was that maybe instead of looking at subtypes, we should start to look at functional subsets and that would help guide therapy. So, as an example, look at all CD30-positive T-cell lymphomas as a group, irrespective of what their subtype is, knowing that we have drugs that attach to CD30; this would be an example. So, again, there's going to be an evolution not only in the name of peripheral T-cell lymphoma, but in the way that we start to think about these disorders and classify them so that we know how to treat patients appropriately.

**[Slide 26 – Communication Among Patients and Healthcare Providers]**

Finally, probably the most important thing, in addition to the doctor talking to the pathologist and the doctor speaking with their patient, is the patient's ability to communicate with their healthcare provider. Open communication with your treatment team is essential to understanding the diagnosis and in helping you make an informed treatment decision. So don't be afraid to ask your treatment team questions. The most important one, I think, would be, "What exactly is my diagnosis? Write it down for me. Is there a standard treatment for my disease? Are you the right doctor to treat my condition? Are there clinical trials available for my condition? Should I get a second opinion?" It's okay to let your doctor know that you'd like a second opinion. Most doctors are used to patients seeking second opinions and even encourage it because let's face it, your life and your health is at stake and it's very, very important that you feel comfortable, that you understand what the treatment options are, and that you've selected the best one for you.

Feel free to speak with your treatment team regarding time and effort commitment. It's actually something that doctors don't always think about but become so important to a patient when they're trying to comply with a time-consuming and maybe complex therapy. "Where are you traveling from? Where are you parking? What kind of work are you trying to do? Is there an important life event coming up for you that you really need to be at?" So these are very, very important things.

At this time, I'll stop talking and allow you to ask any questions that you have, and I will attempt to answer them to my best ability.



## QUESTION-AND-ANSWER SESSION

### [Slide 27 – Question & Answer Session]

#### **Lizette Figueroa**

Thank you so much, Dr. Pinter-Brown, for your very clear and informative presentation.

It is time for our Question-and-Answer portion of our program.

#### **Lizette Figueroa**

We'll take the first question from our Web audience. Brenda asks, "Can peripheral T-cell-NOS, not otherwise specified, come back indolent?"

#### **Dr. Pinter-Brown**

Well, Brenda, that's a really good question. Because PTCL-NOS is a garbage term, what happens sometimes is that someone really has an indolent lymphoma, let's say a primary cutaneous T-cell lymphoma, and maybe it's pretty subtle or it looks like something else, and the doctor doesn't realize it so they biopsy a lymph node or some other more aggressive lesion on the skin. And the pathologist, not knowing the clinical history, not knowing that the person maybe has a skin rash, and for the lack of any better classification calls it peripheral T-cell lymphoma-NOS. So the person may be treated for that entity—that usually means multi-agent chemotherapy—and then relapse somewhere else maybe more now in the skin where people pay attention. They biopsy it and find out it's an indolent lymphoma. But, in truth most of the time, that was present before and people just didn't realize that it was there. So, the answer is that lymphomas and peripheral T-cell lymphomas-NOS are true to their biologic behavior, but what's called peripheral T-cell lymphoma-NOS might not really be if the person reading that slide knew the whole picture of the patient.

#### **Lizette Figueroa**

Thank you, Dr. Pinter-Brown. We'll take the next question from the telephone audience, please.

#### **Operator**

Our next question comes from Jodie calling from Florida. Please state your question.

#### **Jodie**

Hello, Dr. Pinter-Brown. Thanks for taking my call. I was diagnosed with SPTCL or subcutaneous panniculitis-like T-cell lymphoma in 2009. Treated with cyclosporine (Sandimmune®) and prednisone as my main treatment.

My question is I have not had any doctors to date who have treated anybody with this because it's such a rare subtype of a T-cell lymphoma. So I was wondering if there's any way to find out who I could go to possibly in the United States that has more knowledge and has, you know, treated people with this.

**Dr. Pinter-Brown**

That's a good question. So one resource would be The Leukemia & Lymphoma Society but, believe it or not, there's a Cutaneous Lymphoma Foundation and they maintain a list of people who are experts and have expertise and enthusiasm about treating cutaneous lymphomas. And I would kind of put subcutaneous panniculitic lymphoma into that kind of group in a way because it presents in the skin usually first. And so usually the doctors that treat skin lymphomas are the ones that treat this disorder the most.

**Lizette Figueroa**

Thank you, Dr. Pinter-Brown. And as you stated, The Leukemia & Lymphoma Society has an Information Resource Center with Information Specialists who can help you look for a specialist in your area. You can contact them by calling 1-800-955-4572. Thank you.

We'll take the next question from the Web. Mark asks, "My wife complains of fatigue and itching. Is there anything that can help her with these side effects?"

**Dr. Pinter-Brown**

Well, I'll take the one that I can be less helpful with first, I guess, and that's fatigue. The one thing that has been studied over and over again in oncology patients is the use of exercise, particularly walking, for fatigue. And I know that sounds so crazy. If you're fatigued, why would you want to get up and walk? But that's been shown over and over again to help cancer fatigue.

The itching, there have been a lot more kinds studied. So I am assuming that perhaps this person has itching because they have a skin lymphoma; that happens very commonly. And the kinds of things that we generally would think about itching, like antihistamines like if we have a bug bite, actually don't work so well in this situation, but drugs that we use for neuropathies actually worked very well. So things like gabapentin (Neurontin®) is a drug that's used for peripheral neuropathy. It works quite well. A drug called doxepin (Prudoxin™), an old antidepressant, works very well. Also some very simple things can work for itching like just changing the sensation that your skin gets kind of distracts the brain. So putting something cool on the skin is a good example, oatmeal baths is a good example, lubricating the skin is a good example.

So you actually can find resources on the Web and patient advocacy sites. I'll mention the Cutaneous Lymphoma Foundation again just because I know they have a resource on their website where they discuss all the different ways that you can treat itching of the skin because I don't have enough time now to go into all of them. But suffice it to say, there are a lot of different modalities and they're not the usual ones that you would think of.

**Lizette Figueroa**

Thank you, Mark, for your question. We'll take the next question from the telephone audience, please.

**Operator**

Our next question comes from Julie calling from Virginia. Please state your question.

**Julie**

Yes, I was diagnosed in 2009 with anaplastic T-cell lymphoma ALK-positive. And I went into full remission, and I have relapsed in October of last year, actually, with a tumor on my leg like cutaneous lymphoma and systemic as well. I went through ICE (ifosfamide, carboplatin, and etoposide), and I'm in complete remission. And one transplant doctor recommended autologous transplant but then I got a second opinion just to make sure, and another one is recommending allogeneic. Do you have any recommendation? I'm not sure. I'm kind of at a fork in the road. I don't know what's been studied on that.

**Dr. Pinter-Brown**

Yeah, that's a really difficult thing and it shows, again, how little data we have in these situations so that there are some regional differences in what people would recommend.

I think the vast majority of my colleagues would probably recommend auto-transplantation just because it has a lot less morbidity associated with it, and there are studies looking at auto-transplantation in relapsed and refractory peripheral T-cell lymphoma where the patients with ALK-positive anaplastic large-cell lymphoma seem to do better than the other groups of patients. So there actually is some literature—not a lot—but there is some literature to support that. It doesn't mean that allogeneic transplant is wrong. There's just not very much information about it. So most people would vote with the data that we do have showing that this is an efficacious way to treat patients with anaplastic large-cell lymphoma ALK positive in relapse once they've attained a complete remission.

**Lizette Figueroa**

Thank you. We'll take the next question from our Web audience. Carmen asks, "What is the current status of vaccine therapy in trials for PTCL?"

**Dr. Pinter-Brown**

Sadly, I know of no vaccine trials going on in T-cell lymphoma. Part of the problem is that you use your T-cell immunity to respond to vaccines, and many patients with T-cell lymphoma don't have normal T-cell immunity. That is their normal T cells aren't really totally normal. However, different kinds of immune therapies are being evaluated that might stimulate the immune system in a way that a vaccine would and to try and keep control of the disease, but these are in very, very early stages at this time.

**Lizette Figueroa**

Thank you. And we'll take the next question from the telephone audience, please.

**Operator**

Our next question comes from Jane calling from Delaware. Please state your question.

**Jane**

Yes. I have a peripheral T-cell lymphoma, was on the CHOP and then I had a stem cell, which I had another reoccurrence shortly after the stem cell and I am on rituximab right now. Do you think that's the best way to go, and would there be other stem cell replacements down the road do you think?

**Dr. Pinter-Brown**

Many patients would consider an allo-transplantation if they had an auto-transplant to begin with. Many transplant centers, however, want to make sure that the disease is well under control for a long period of time before attempting that. And there are, as I mentioned, a number of ways of getting into a complete remission so that that could be considered.

So to have an allo-transplant, obviously, a donor needs to be found. And it sounds as if all things were equal and you were a candidate for allo-transplantation, that this might be a good time to look and see if there is a donor and if that is an option for you in the future.

**Jane**

Okay, so even though my first stem cell was from my own stem cells, the next time would be probably from a donor is what you're saying, if I had another one.

**Dr. Pinter-Brown**

Right. So you bring up a good point and a general one, which is what's the difference between an auto- and an allo-transplant? They're done with really different purposes in mind. In an auto-transplant, the stem cells come from the person themselves; they haven't been changed in any way. And the real point of an auto-transplant is that big doses of chemo or chemo and radiation is given before the cells are returned. And that's really the treatment, the chemo and the chemo or radiation.

In an allo-transplant, where cells come from someone else, the purpose is really different. The purpose is to give the patient somebody else's immune system that may not be so tolerant of having lymphoma cells in that body. So, yes, there is chemotherapy or chemo and radiation before that kind of transplant, but it's really to prepare the person to accept someone else's stem cells and accept someone else's immune system. The real point is to develop a new immune system, not the chemotherapy. So even though they're both called transplants, they're done with totally different purposes in mind and they have different side effects for that reason.

**Lizette Figueroa**

Thank you so much for that clear and concise answer. We'll take the next question from the Web. Harry asks, "At what point do you recommend a clinical trial? In your opinion, should patients try standard or proven methods first?"

**Dr. Pinter-Brown**

Well, as I mentioned, unfortunately, in peripheral T-cell lymphoma, we don't have a lot of proven methods, so clinical trials are very, very important and sometimes will offer a more promising therapy than the standard. So I think it has to be individualized. Obviously, the NCCN says, "Everybody should be in a clinical trial," and that is how we're going to learn what to do and what the proven treatments are. But I think in an individual's case, they should be looking at what clinical trials are available and weighing that against what's offered as a standard and seeing if, really, maybe the clinical trial offers more promise.

**Lizette Figueroa**

Thank you, doctor. And, also, at the Information Resource Center, we do have Information Specialists who can conduct individual clinical trial searches for you. You can reach them by calling 1-800-955-4572 or emailing them at [infocenter@lls.org](mailto:infocenter@lls.org).

We'll take the next question from the telephone audience, please.

**Operator**

Our next question comes from Betty calling from Florida. Please state your question.

**Betty**

Yes, doctor. Does malignant mastocytosis have any relationship to this peripheral T-cell lymphoma?

**Dr. Pinter-Brown**

No, it really doesn't. Mast cells, though they're in the skin, are really different cells. They're not lymphoid cells and they're the cells that are, though they're part of our immunity, are responsible for us having hives, as an example, because they release their contents. And they have very different treatments.

**Betty**

Okay, thank you, doctor. Appreciate your answer.

**Lizette Figueroa**

Thank you for the question. We'll take the next question from our Web audience. Zee asks, "Is there a replacement or successor for Ontak® (denileukin diftitox) since it was withdrawn at the end of 2013?"

**Dr. Pinter-Brown**

Good question. All right, so denileukin diftitox was a fusion protein where a Diphtheria toxin was altered so that it would only attack certain cells with interleukin (IL)-2 receptors. And there actually are ongoing trials with a drug that is like denileukin diftitox. It's called E7777. So that if you go onto [clinicaltrials.gov](http://clinicaltrials.gov) and put E7777 in, you will see where the clinical trials are ongoing. And then we'll see if the drug gets FDA approved.

**Lizette Figueroa**

Thank you. That's hopeful news. And we'll take the next question from the telephone audience, please.

**Operator**

Our next question comes from Jeannie calling from New York. Please state your question.

**Jeannie**

Hi, doctor. Is there ever any time where Revlimid® (lenalidomide) might be used for any of the peripheral T-cell lymphomas, because I read about it in an article?

**Dr. Pinter-Brown**

Lenalidomide has been studied for peripheral T-cell lymphomas in general. There's probably more literature about angioimmunoblastic lymphoma where there's literature regarding thalidomide (Thalomid®), which is the drug that lenalidomide emerged from, in the treatment of that disorder. But there is medical literature and some phase II trials looking at other T-cell lymphomas in relapsed/refractory state, and the response rate is around 30%.

There's also a proposed study upfront adding lenalidomide to chemotherapeutic agents to see if this might be a better way to initially treat patients with peripheral T-cell lymphoma than using CHOP or CHOP-like agents.

**Lizette Figueroa**

Thank you, doctor. And the next question we'll take from the Web audience. Bridgette asks, "Can you comment on the role of autologous and allogeneic stem cell transplant, and also the rationale for autologous transplant followed by an allogeneic transplant? I'm in remission and it was recommended to me to get an autologous transplant followed by an allogeneic transplant."

**Dr. Pinter-Brown**

So I'll start with that. Some institutions have had the idea to use an autologous transplant to reduce the number of tumor cells and then follow it with an allogeneic transplant to, again, adapt somebody else's immune system that now won't have to work against such a lot of cells. I think the rationale for that is that sometimes people have peripheral T-cell lymphomas and they relapse quickly. And this is a way to reduce the number of cells so that the patient has approximately the three months necessary for the adopted immune system in an allo-transplant to actually be strong enough to do anything. So it takes a while for that adopted immune system to be strong enough to actually affect control of lymphomas.

This definitely is a research question and would be undertaken in a research trial. We talked about the difference between auto- and allo-transplantation, and I did mention that there are some institutional or geographical preferences. Some institutions favor allo, some auto, some none at all. I think, in general, the majority of institutions favor auto-transplantation; however, there are some particular subtypes of T-cell lymphoma that are so highly refractory to chemotherapeutic agents that an allo-transplant might be suggested upfront because the center would be worried that if they did an auto-transplant and the person relapsed that they would not be effectively able to get them back into a remission, which is always necessary before transplantation.

**Lizette Figueroa**

Thank you so much for the question, Bridgette. And we'll take the next question from the Web audience. Nancy asks, "I've heard that brentuximab vedotin is being studied in children with relapsed systemic anaplastic large-cell lymphoma. Are there any results from these studies?"

**Dr. Pinter-Brown**

Actually, results were just presented at the recent American Society of Clinical Oncology (ASCO) meeting [June 2014] and there have been results published before. There is a phase I/II study of brentuximab vedotin in children who have anaplastic large-cell lymphoma. In the phase I portion, what dose should be used and what the side effects are is the one that was published.

**Dr. Pinter-Brown**

So, it turns out that the dose was pretty much the same as adults. The toxicities were similar. However, when I looked at the toxicities, what struck me is that children seem to have a little more in the way of nausea and abdominal pain than adults do who experience neuropathy or numbness or tingling in their fingertips or toes more frequently. But, certainly, there is an ongoing phase II portion of this to know how well it works, but there's already information, thankfully, to show that it is safe to use in children.

**Lizette Figueroa**

Great. Thank you for that question. We'll take the next question from the Web. Ed asks, "Are mycosis fungoides and Sézary syndrome the same?"

**Dr. Pinter-Brown**

Really good question. So, the way it currently stands, mycosis fungoides is kind of an umbrella term and Sézary syndrome is a subset of patients within that diagnosis that usually have complete redness of their skin and have a significant number of the malignant cells floating around in their blood that is a leukemia, if you will. But in future, there is information that they are not exactly the same cells of origin. And in future, again, as I mentioned, the classification changes all the time. We may recognize Sézary syndrome as a separate condition.

**Lizette Figueroa**

Thank you. And we'll take another question from the Web audience. Allison asks, "Are there any drug interactions to look for with brentuximab vedotin?"

**Dr. Pinter-Brown**

The primary one is a chemotherapy, bleomycin (Blenoxane®); it seems to cause a lot of lung problems when it's used with brentuximab vedotin. And the other are what's called cytochrome P450 (CYP)3A4 inhibitors or inducers basically. All those admonishments that you see when somebody says, "Don't drink grapefruit juice, don't drink pomegranate juice or noni juice or use St. John's Wort," these have some of the things that affect this enzyme. And then there's a very long list of drugs which you could get probably off the Web, even in Wikipedia, of drugs that affect this particular enzyme.

The use of those drugs, though, however, may not mean that brentuximab vedotin can't be used, but just that people have to look at it and be maybe more attentive to if there are side effects so that the dose might be modified effectively.

**Lizette Figueroa**

Thank you, doctor. And we'll take the next question from the telephone audience.

**Operator**

Thank you. Our next question comes from Alice calling from Louisiana. Please state your question.

**Alice**

Yes, I was diagnosed with large B-cell non-Hodgkin's lymphoma in early '09 and I had a number of drug treatments and two years of rituximab. And along with the rituximab while I was doing it, I was continuously reading about my condition. And I researched as much as I could on the Web about it. And I ran into this German chemist by the name of Dr. Johanna Budwig who stated that this had been successfully treated with flaxseed oil and cottage cheese organic. And I did tell my oncologist that I was using it. And it did very well with me, but what they didn't tell me was after the rituximab that I would be so tired; I read that. And to even this day I'm very, very tired. More tired today than I was when I was doing the chemo and the rituximab, and I couldn't understand that. And also read that rituximab was linked, has been linked to a deadly brain disease. Had you heard that? And if so, what is it that I can do about my tiredness?

**Dr. Pinter-Brown**

I'm sorry, linked to what?

**Alice**

Rituximab has been linked to a deadly brain disease.

**Dr. Pinter-Brown**

Oh, okay. So since we're talking about T-cell lymphomas, let's kind of turn this into a general question. So I think, let's talk about the brain disease thing. So some of us have what's called preons in our brain and they're latent. That means they're not doing anything. And any time someone becomes immunosuppressed, sometimes this can become a disease, and that's what you read in the package insert. It doesn't just happen with rituximab. It can happen with other forms of suppression of the immune system. So the larger question, I guess, is fatigue, which we talked a little bit about. And then the third question you raise is about flaxseed oil or cottage cheese. And those things, unfortunately, we don't have trials to inform us how helpful they are, but I think that many, many patients use different kinds of adjunct treatments, and the important thing would be to mention it to the physician so that they make sure that it doesn't interact with anything else that you might be taking.

**Lizette Figueroa**

Thank you so much, doctor. And we'll take the next question from the Web audience. Lee asks, "What are some treatment options for CD30-positive ALCL other than methotrexate? I have concerns about adverse effects that may arise from a seven-year course of methotrexate."

**Dr. Pinter-Brown**

Are we able to clarify if we're talking about cutaneous CD30-positive anaplastic large cell? Or we don't know?

**Lizette Figueroa**

I'm sorry, it's a Web question.



**Dr. Pinter-Brown**

Okay, so I'm going to make an assumption that you're talking about a disorder that's in the skin because methotrexate would be a treatment for that. Well, there is this trial, as I mentioned, with brentuximab vedotin, and many patients are able to get that drug off of trial as well. Additionally, sometimes some of the treatments used for other primary cutaneous lymphomas, like bexarotene can additionally be used.

**Lizette Figueroa**

Thank you. Now we'll take the next question from the telephone audience.

**Operator**

Our next question comes from Jennifer calling from New York. Please state your question.

**Jennifer**

Thank you, doctor. You listed radiation under the treatment options. Is that only during transplant or is it sometimes used alone?

**Dr. Pinter-Brown**

It's usually not used alone. It's, in some institutions, used in conjunction with chemotherapy in certain cases.

**Lizette Figueroa**

Thank you. And we'll take the next question from the Web. Chris asks, "Do you know of any specific treatments for recurring enteropathy-associated T-cell lymphoma (EATL) type II?"

**Dr. Pinter-Brown**

Well that, as you saw, was listed in the specific treatment. So I guess if I had a person like that, I would look to see what their initial treatment was because there is a regimen that is often used in that situation. We call it the Newcastle regimen because it was published by a group in Newcastle in the UK. Other than that, the drugs that would be used for peripheral T-cell lymphoma might also be useful in enteropathy type T-cell lymphoma.

**Lizette Figueroa**

Thank you. And we'll take the next question from the Web. Kevin asks, "How often should a patient in remission from anaplastic large T-cell lymphoma be getting positron emission tomography (PET) or computed tomography (CT) scans, or is it just a physical exam on the lymph nodes that's needed?"

**Dr. Pinter-Brown**

That's a really good question. I think there's been a change in paradigm more recently in the world of lymphomas, not specifically for T-cell lymphomas because we don't have that information in T-cell lymphomas; but what's been found for a long time going back to when we just had CT scans moving forward to when we have PET CT scans, is that the majority of the time when a patient relapses, the patient is aware of some change in their symptoms. And as they report it to the physician, the physician then is concerned about a relapse and orders scanning. Sometimes relapses are also found by the physician in doing physical examination or laboratory testing. So, really, a minority of patients' relapses will be picked up solely on surveillance scanning leading many of us to dismiss

surveillance scanning and rely more on listening to what the patient feels and examining them and doing laboratory work. And then deciding, based on that knowledge, whether the patient really needs a scan at that time to try and find a relapse.

**Lizette Figueroa**

Thank you. And we'll take the next question from the Web. Patricia asks, "Since PTCL is uncommon, are there resources to help me connect with others who can relate to what I'm going through?"

**Dr. Pinter-Brown**

I'm going to turn this over to the LLS because I know they have programs and know more about how patients might access those.

**Lizette Figueroa**

Sure, of course. And thank you, Patricia, for your question. We definitely would like to invite you to take part in the LLS' support services. We have in-person family support groups, online chats that are facilitated by oncology social workers, and our Patti Robinson Kaufmann First Connection Program that actually connects you with a peer volunteer who has been treated for the same diagnosis. So, again, Patricia and all of you, for information on any of these programs, please contact our Information Resource Center at 1-800-955-4572.

We have time for one more question, doctor. And this is from Susan. She says, "I'm on pralatrexate for PTCL and was wondering if I can get a shingles vaccine."

**Dr. Pinter-Brown**

Oh, good question. Well, in theory, the current shingles vaccine that's on the market is live, and what it says in its package insert is that anyone who has lymphoma or has had lymphoma should not receive that vaccine. There is a theoretic concern because people with lymphoma often do not have totally normal immune systems that this live virus vaccine could actually make them sick.

There are current trials looking at a vaccine that would be safe in patients with lymphoma, but currently that vaccine is not on the market. So my recommendation would be, no, do not get the shingles vaccine.

**Lizette Figueroa**

Thank you, doctor. I know that's been something that a lot of our patients have asked us. And thank you all, for all of your questions.

## CLOSING REMARKS

[Slide 28 – The Leukemia & Lymphoma Society (LLS) offers]

### *Lizette Figueroa*

We hope this information will assist you and your families in your next steps. The Leukemia & Lymphoma Society offers online chats for patients with non-Hodgkin lymphoma and chats for young adults and caregivers. These chats are moderated by oncology social workers and they provide a forum for patients and caregivers to share experiences and support for each other. For information on how to participate, please review the flyer in your packet, or you can go to [www.LLS.org/chat](http://www.LLS.org/chat).

If we weren't able to answer your question today, please call The Leukemia & Lymphoma Society's Information Specialists at 1-800-955-4572. Information specialists are available to speak with you from 9 AM to 9 PM Eastern Time. And these are new expanded hours, so please call an Information Specialist with your questions, or you can reach us by email at [infocenter@lls.org](mailto:infocenter@lls.org). We can provide information about treatments, including clinical trials, or answer other questions that you may have about support, including questions about financial assistance for treatment.

Please help me thank Dr. Pinter-Brown for volunteering her time with us today. On behalf of The Leukemia & Lymphoma Society, thank you all for sharing your time with us. Good-bye, and we wish you well.