PTCL–Diagnosis and Treatment Update | May 29, 2013

LEUKEMIA & LYMPHOMA SOCIETY®
fighting blood cancers

Speaker: Julie M. Vose, MD

Slide 1: Welcome and Introductions

OPERATOR:
Hello, everyone, and welcome to *PTCL–Diagnosis and Treatment Update*, a free telephone/web education program. It is my pleasure to introduce your moderator Lauren Berger of The Leukemia & Lymphoma Society.

LAUREN BERGER:
Thank you and hello, everyone. On behalf of The Leukemia & Lymphoma Society, a warm welcome to all of you. Special thanks to Dr. Julie Vose for sharing her time and expertise with us today.

We have over 330 individuals participating from across the United States and also from Barbados, Canada, China and Sweden.

We'd like to acknowledge and thank Celgene Corporation for their support of this program.

I am now pleased to introduce Dr. Julie Vose, Neumann M. and Mildred E. Harris Professor and Chief, Division of Oncology/Hematology, at the Department of Internal Medicine, University of Nebraska Medical Center in Omaha, Nebraska. Dr. Vose, we're so privileged to have you with us today, and I'll now turn the program over to you.

Slide 2: Treatment and Clinical Trials for PTCL

DR. JULIE VOSE:
Thank you very much. I really appreciate the opportunity to speak with everyone today.

What I'm going to do is try to put T-cell lymphoma a little bit into context with respect to the other types of lymphomas, talk about current treatments and what we look for, for issues with respect to patients, what their prognosis is, and then talk about some of the new treatments that are either accessed recently or in clinical trials.

Slide 3: 2013 Estimated U.S. New Cancer Cases
So just to talk about cancer in general, to put things into context, non-Hodgkin lymphoma is the fourth or fifth most common type of cancer that we see. This slide shows the updated information from 2013, estimated U.S. new cases. And you can see that non-Hodgkin lymphoma is about 4% of all the types of cancers. In men the most common type would be prostate cancer. In women the most common type would be breast cancer. And this just kind of puts it into context with the other types of cancers that we see.

Slide 4: Most Common Subtypes of NHL
The next slide shows you some of the more common types of non-Hodgkin lymphoma and again to try to put the T-cell and NK cell lymphomas into context. The most common type of lymphoma that we see in the United States is called diffuse large B-cell lymphoma. That represents about 30% of all non-Hodgkin lymphoma. That's shown in the green in the bottom of the slide, in the pie. Next most common type would be follicular lymphoma, about 25%, that's in yellow. And that's a type of lymphoma that we see fairly commonly in the United States, but is not seen in some of the underdeveloped countries as commonly.

DR. JULIE VOSE:

Slide 5: T-cell Lymphomas
T and NK cell lymphoma, which is our topic today, represent somewhere between 10 and 15% of all non-Hodgkin lymphoma, so it's fairly common in respect to some of the different types of lymphomas, but there are many different types of T-cell lymphomas, as we'll get into a little bit later.

Slide 6: Classification of Peripheral T-cell Lymphoma (PTCL)
This slide shows us some of the classification of peripheral T-cell lymphoma. And so a common misnomer is that when people say peripheral T-cell lymphoma or PTCL, they think that that has to mean that it's in the skin or in the periphery, but that's not the case. Although many times this type of lymphoma can involve the skin. So this classification system just shows us the different types of lymphomas. The biggest classification is B-cell versus T-cell. T-cell being the 10 to 15% we're talking about today. And then within the T-cell or NK cell types of lymphomas, there are two major classifications, a precursor or early T-cell and that one's called lymphoblastic lymphoma or leukemia, and the mature T-cell or NK cell type of lymphomas, and those have four different major classifications with respect to the area that they're located. One would be cutaneous, that's where many of the T-cell lymphomas are in the skin or involved with skin plus other places. One would be called extranodal and that's where the lymphoma is outside of the lymph nodes and other organs. Nodal, which means that the lymphoma is located within the lymph nodes for the most part. And leukemic, where the type of lymphoma is located mostly in the blood and the bone marrow. And these are just four major kind of buckets, if you will, to put the different types of lymphomas within the T-cell category.

Slide 7: Distribution of 1,314 Cases by Consensus Diagnosis
This next slide is from a very large international study that we did and published a few years ago, looking at over 1,300 newly diagnosed cases of T-cell lymphoma at 22 centers worldwide. And this breaks down the different types of T-cell lymphomas. And even since this was published we have learned more and understand more of the different subtypes of T-cell lymphomas.

But in general the most common type of T-cell lymphoma that's diagnosed is called peripheral T-cell lymphoma, not otherwise specified. We now know that there are probably at least three major subtypes within that kind of bucket category, as we're learning more and more in our research.

The second most common type of T-cell lymphoma is called angioimmunoblastic T-cell lymphoma. And this is about 19%. The PTCL NOS is about 26%.

Angioimmunoblastic T-cell lymphoma has some very specific types of things that patients can present with when they're first diagnosed. One is commonly a rash. Lots of times patients have enlarged lymph nodes, may have an extra abnormal type of protein in their blood, may have a type of anemia called hemolytic anemia. So it's a very specific type of lymphoma that we see typically in that category.

You can see the other types of T-cell lymphomas. Some of them are quite rare and because the numbers are so rare, it's hard in some cases to find physicians that have seen a lot of these types of patients, unless they have a specialty in T-cell lymphoma.

DR. JULIE VOSE:

Slide 8: PTCL Incidence
The next slide goes over some of the increasing incidence of peripheral T-cell lymphoma. And you can see on the left-hand side, in the yellow line there, all cases of peripheral T-cell lymphoma of any different type have been going up and have been diagnosed more over the last several years and couple of decades. Now some of this may be due to the fact that we're recognizing this more commonly. Also that our population is aging and most lymphomas in general, and T-cell lymphomas, occur in older patients. But whatever the reason, we are recognizing this more commonly throughout the world and specifically in the United States.

Slide 9: Staging of PTCL
The next slide goes over staging of peripheral T-cell lymphoma. So the first thing that we do when we have that diagnosis would be we want to find out the extent of the lymphoma, because that really is helpful in trying to form the different treatments that we may suggest for the patient. So we may do studies such as a CAT scan, in some cases a PET scan, bone marrow biopsy, and other tests as appropriate to find the location of the lymphoma.

And as with other types of lymphomas, this is broken down into different stages. Stage I is that the lymphoma is just in one location, typically in the lymph nodes, but can be outside the lymph nodes. Stage II would be the cancer, in this case lymphoma, is in two separate locations, but on the same side of the diaphragm, so that means either usually in the chest or neck area or alternatively below the diaphragm in the abdomen or groin area. Stage III means that the lymphoma is both above and below the diaphragm. And Stage IV means that the lymphoma is diffuse or disseminated, involves one or more extranodal, extralymphatic sites, that could be in any of the organs such as the liver, spleen, bone marrow, lungs, multiple locations in the skin, would make the patient a Stage IV.

There are a couple of modifiers that we look at. A would be not any constitutional or B symptoms present. B means that there are some B symptoms present and B symptoms consist of weight loss greater than 10% over the ensuing six months, prior to the diagnosis; if the patient has drenching night sweats on a consistent fashion that are not associated with another diagnosis such as menopause; and if the patient has consistent fevers that are over 101.5 on a cyclical or multiple day, multiple week, multiple month history, then that would be the presence of B symptoms. E means extranodal disease, if it's outside of the lymph nodes.

So when we see the person we're going to use this information to develop a stage classification for the patient, we want to make sure that the biopsy is done by expert hematopathologists, to be sure that we know exactly the type of lymphoma, because we often see patients who maybe come from an area that they're not used to seeing very many lymphoma patients, that they don't really know maybe the ups and downs of the newer classification system. So those two things are really kind of the first things that we work out when we see a new patient with lymphoma.

Slide 10: Prognostic Indices for PTCL
The next slide goes over some of the other information that we look at to try to develop a plan for the patient's care. And in this case we're going to look at what's called prognostic indices. So we look at some very simple things. Perhaps the age of the patient, sometimes a blood test such as the lactate

DR. JULIE VOSE:
dehydrogenase or LDH. We look at how well the patient is able to perform their normal activities, the extent of the lymphoma, stage, that we just talked about, and if the lymphoma is outside the lymph node system or if it has bone marrow involvement. Putting all these factors together helps us to evaluate, based upon a population evaluation, what the potential outcome for the patient is, based upon prior information.

So if the patient has zero of these factors, they can expect to have a better potential outcome than if the patient has many of these factors. And unfortunately for patients with peripheral T-cell lymphoma, they often have many of these factors and therefore our information, at least in the past, has demonstrated that patients with peripheral T-cell lymphoma with standard treatment do not do as well as patients with other types of lymphomas.

Slide 11: The International PTCL and NK/TCL Study: OS in PTCL
This slide is also from the international T-cell project, which took the 1,300 patients we talked about earlier, and looked at the outcomes for the patients based upon standard treatments that they received at the center they were treated at. And you can see, this is using what's called a Kaplan-Meier curve, and looking at the survival of patients and the years of time. And then we looked at the different types of lymphomas, and you can see some types of lymphoma, such as anaplastic large cell lymphoma, do quite well, with about 70% of the patients alive and doing well at five years after their diagnosis, or many years after. Some of the other types of lymphomas that are more rare, the patients do not have as good an outcome and we're always trying to look for better options for all of our patients.

Slide 12: NCCN Guidelines for Initial Treatment of PTCL
Now this slide shows what's called the NCCN guidelines, or National Comprehensive Cancer Network guidelines, for the initial treatment of peripheral T-cell lymphoma. The NCCN is a group of about 20 large cancer centers and we're included in that, as well as many large cancer centers throughout the United States, that have developed guidelines for treating patients with all different types of cancers, but in this case lymphoma. And this is based upon information that's in the literature, information at the large cancer centers, and looking at what's the best opportunity for patients with different types of cancers.

In this case, specifically for peripheral T-cell lymphoma, anaplastic large cell lymphoma, ALK-positive, which is a common type that we see in the United States, is fairly well treated with some of our standard therapies such as CHOP, given every 21 days, or CHOP plus the addition of etoposide, given every 21 days. And you can see that's the recommendation for induction therapy. And no additional consolidation therapy is needed.

However, many of the different types of peripheral T-cell lymphoma, other than anaplastic large cell lymphoma, do not do as well with standard therapy. And you can see based upon these guidelines that the number one preferred choice of therapy for those patients is clinical trial. That means that we're always trying to look at additional types of therapies to add to our current standard of therapy or instead of, to try to see if we can improve the outcome for these patients. So definitely if peripheral T-cell lymphoma is a diagnosis, we want to try to consider that at the time of their first diagnosis for patients or subsequent treatments.

DR. JULIE VOSE:
We also do consider using high-dose therapy and stem cell transplantation for patients after their induction therapy, for higher risk peripheral T-cell lymphoma patients. And some studies have demonstrated improved outcome when using this as a consolidation type treatment.

Slide 13: Adding Etoposide to CHOP
So the two areas that we've seen perhaps can improve the outcome for patients with peripheral T-cell lymphoma using current standard treatment options would include the addition of one agent, etoposide, or VP-16, to a standard CHOP or CHOP-like regimen, which includes other agents that we normally use for chemotherapy, such as Cytoxan®, Adriamycin®, vincristine and prednisone, and this was based upon studies that were performed in Germany. You can see on this slide that the addition of this drug etoposide appeared to improve the outcome for patients with peripheral T-cell lymphoma specifically. And this is an agent that we now are combining in many cases with standard chemotherapy to try to improve the patient's outcome with T-cell lymphoma.

Slide 14: German Prospective Trial of ASCT in First Remission
The other area that appears to also improve the outcome for especially high-risk patients is noted on this next slide. And this is again a study from Germany, but there are several other studies looking at the use of stem cell transplantation, using a patient's own stem cells or autologous transplant, that are collected out of their blood. Patient undergoes standard chemotherapy and then, once a remission has been obtained, patient then goes under high-dose chemotherapy and receives his or her own stem cells back. And it appears this additional consolidation treatment can help the patients, especially the higher risk patients, to improve their outcome. So this is often part of our treatment plan or clinical trial that we might evaluate or say that the patient may benefit from.

Slide 15: NCCN Treatment Guidelines for Relapsed/Refractory PTCL
Now if the lymphoma were to come back, despite our best efforts, then we need to look at additional types of treatments and these again are from the NCCN treatment guidelines for patients with relapsed or refractory peripheral T-cell lymphoma, if it comes back after the initial therapy. And you can see that again at the top of the list, both for patients that are or are not stem cell transplant candidates, that clinical trial is always preferred because we're always trying to look for the best possible treatment and clinical trials typically offer newer drugs or newer combinations of drugs and also keep track of patients, so that we can understand how these new treatments are working.

You can see there are a long list of other potential treatments that are listed here that have been shown to have some activity with T-cell lymphoma, so these may also be options in some specific patient. Each patient needs to be looked at individually, what might work best for that patient.

Slide 16: Relapsed/Refractory PTCL
Now we are fortunate that there have been three new drugs that have been FDA approved over the past few years for T-cell lymphoma. I'm going to go over those just briefly. One is romidepsin, which is an in-the-vein chemotherapy. One is pralatrexate, which is also an in-the-vein chemotherapy. And one is called brentuximab vedotin or SGN-35, and that particular medication is for a very specific type of T-cell lymphoma, anaplastic large cell lymphoma, and that one is actually an antibody or protein that attaches

DR. JULIE VOSE:
to the lymphoma cell and then attaches to that protein is a form of chemotherapy. So those three have been approved over the past few years for T-cell lymphoma. And I'll go over a little bit more information about each of those.

Slide 17: Pralatrexate Mechanism of Action
So pralatrexate was the first one that was approved and this is a medication that's similar to an old medication we had, methotrexate, and this is what we call an antifolate chemotherapy drug. So this is one of the newer drugs that we have, that's sort of a next version of an older drug. The advantage that pralatrexate has, that it selectively enters the malignant cells as opposed to the normal cells, accumulates inside the cancer cells, as is demonstrated on this slide, and then is able to interrupt some of the growth pathways of the cancer cell and triggers cancer cell death.

Slide 18: PROPEL Study
This medication is given in a few different ways, but the way that it's approved is for it to be given once a week for six weeks and patients do need to receive vitamin B12 and folic acid while on this particular medication, to try to prevent a side effect of sore mouth or mucositis.

This medicine is FDA approved now and is used either alone or sometimes in combination with other drugs in a clinical trial. And about 30% of patients with peripheral T-cell lymphoma that have failed other therapies can respond to this agent. It would not be a curative treatment, but would be one that can hopefully put patients into remission, at least for a while.

Slide 19: Depsipeptide in Relapsed/Refractory PTCL
Another new drug that we have over the past few years is called depsipeptide or romidepsin. And this again is approved for patients with relapsed or refractory peripheral T-cell lymphoma. It's given weekly in the vein for three weeks out of four weeks and typically the major side effects of this are slightly low blood counts and fatigue for patients. Again, works in about 30% of patients with peripheral T-cell lymphoma that's relapsed.

Slide 20: Brentuximab Vedotin Mechanism of Action
The other new agent that we have available for a specific subtype of T-cell lymphoma anaplastic large cell lymphoma is called brentuximab vedotin or SGN-35. And this is a monoclonal antibody or a protein that is given through the vein. Attached to this protein as a biolinker system is a potent antitubulin chemotherapy agent. So what happens is the antibody attaches to the lymphoma cell, based upon this surface receptor, it's drawn into the cell and then the chemotherapy drug is released once the antibody is in the cell and causes cell death, just to the cancer cell and not of the non-cancer cells. So it has the same effect on the cancer, but less side effects for the patient. And this is a new technology that's also being applied to other types of antibodies and other types of chemotherapy as well.

Slide 21: Targeting T-cell Lymphoma
But we're always looking for new ways to try to attack the T-cells. And this slide just shows different ways that we're looking at trying to potentially attack the T-cell lymphoma, either by surface markers, such as these antigens on the surface of cells that bring the antibodies or proteins closer to the cancer cells

DR. JULIE VOSE:
themselves, in this case T-cells. Another way is by trying to interrupt the environment that the lymphoma lives in, so in this case the lymph node or the bone marrow or the spleen, that lymphoma really relies upon extra cells to try to keep it alive, and so this is a way to try to interrupt that. Also different pathways within the cells themselves, to try to interrupt the growth of the cells.

Slide 22: New Agents for T-cell Lymphoma
Next slide shows a lot of different potential types of either chemotherapies or antibodies or these pathway-directed cells that we're looking at for potential agents to fight T-cell lymphoma. And it may be that perhaps one of these individually is not going to work, but we may be able to combine these together or sequence them together, to improve the outcome for patients with T-cell lymphoma.

Slide 23: Alisertib: Investigational Aurora A Kinase Inhibitor
Just want to talk about a couple of new treatments that are showing some promise. These are in clinical trials, they're not yet available. One is called alisertib and it's what is called an aurora kinase inhibitor. And this particular agent is an oral agent and it interrupts a specific pathway in the T-cell. It was found very early on that this worked in all types of lymphomas, but appeared to have a pretty high response rate in T-cell lymphomas, which has led to a larger clinical trial that's currently ongoing. So there's no information or data available for that as of yet.

Slide 24: Anti-CCR4 Antibody: KW-0761
Another new antibody that is available for some types of lymphomas and currently in clinical trials in the United States would be what's called an anti-CCR4 antibody. And this specifically has been tested in patients with acute T-cell leukemia/lymphoma, and that's most commonly seen in Japan or the Caribbean, and is very highly effective in those patients. It also appears to work in about 30 to 40% of patients with peripheral T-cell lymphoma and it's currently undergoing Phase II and Phase III studies in the United States, to see if it can be as good or better than some of the currently available treatments.

Slide 25: Lenalidomide in Relapsed/Refractory Aggressive NHL: Results
Another new type of treatment that's currently in some clinical trials or has activity in T-cell lymphoma is called lenalidomide or Revlimid®. This is also an oral medication. It's currently approved for use for patients with multiple myeloma and myelodysplastic syndrome, so two different types of bone marrow disorders. But has been found in some small trials to have some activity in T-cell lymphoma. This study shows that patients with peripheral T-cell lymphoma, about 45% of patients did have a short response with this agent, and it's being looked at either alone or in combination for potential treatment of peripheral T-cell lymphoma.

Slide 26: Gene Expression Profiles (GEP) in PTCL-nos
Now what about the future, where do we go with this? Well, what we'd like to do is to be able to identify specific types of patients that have the different subtypes of T-cell lymphoma, and then to be able to do some genetic analysis of the lymphoma, to see what the best treatment may be. There's a little bit of information that has been out there, looking at this type of what's called gene expression profiling, and that's where we take a sample of the lymphoma and do some special studies in the laboratory, to find

DR. JULIE VOSE:
out which pathway or which genes may be targeted in that individual patient. Now this is all in the research realm, it's not anything that's clinically available, but I think this is probably the way of the future. So if you find a clinical trial that perhaps can utilize some of this type of gene expression profiling, you'll potentially not only be helping yourself, but also be helping patients in the future.

So this is just some work that has been done at a couple of different centers now, showing that there probably are at least four different types of peripheral T-cell lymphoma, not otherwise specified, based upon that big category. And that perhaps there's some specific genes in some of these subtypes that we can target with our new therapies.

So for example, this study that was done showed three different subtypes of peripheral T-cell lymphoma and subtype 2, it looked like that particular pathway, what we call NF-kappa-B may be important, so that has led to some clinical trials in NF-kappa-B inhibitors. And in subtype 3, it looks like there are some genes that are overexpressed that are in the JAK/STAT pathway, so that has led to some clinical trials of drugs that actually inhibit that pathway in specific types of T-cell lymphoma. So you can see this research information is really helpful not only for the patients that are on the current clinical trials, but also patients in the future, to try to see if we can improve upon our treatments.

Slide 27: Future for PTCL Therapy
So what does the future hold for patients with peripheral T-cell lymphoma in the therapies? Well, I think we can tell from our current information that standard chemotherapy unfortunately does not work very well and we need to find new treatments, either combinations or sequential treatments or different types of treatments that are helpful for this type of lymphoma. And that's probably going to mean that we're going to have to do some additional studies with this gene expression profiling or other clinical trials associated with laboratory studies, to see how we can identify the best treatment for these patients.

It also means that we probably are not going to be able to use just one treatment for lymphoma like we do with some of the other lymphomas, that we have to use different types of treatments, maybe in sequence or consolidation, to be able to improve our patients' outcomes. So you see a lot of the clinical trials now have combinations of what's called induction therapy, maybe six cycles of standard chemotherapy, a consolidation, maybe there's stem cell transplant done after that, and then maybe even a maintenance therapy or an oral medication, to try to keep patients on after that time, to keep them in remission, because this is a more difficult type of lymphoma to treat.

As I talked about earlier, we do consider transplantation for selected younger patients with this type of lymphoma as an option. It's not the option for everybody, but in some patients it may be appropriate. Always looking for new treatments to try to see if we can improve the outcome for these patients with peripheral stem cell transplantation also as an option, even in addition to that. And most importantly, clinical trials, because that's really the only way that we can see what the best treatment for patients with T-cell lymphoma is, if we get patients that do participate in clinical trials and help us to formulate treatments, not only for themselves, but also for future patients.

Thank you very much and I think we'll have plenty of time for questions. I'm going to turn this back over to Lauren for the question and answer period.

Slide 28: Question and Answer Session

LAUREN BERGER:
Thank you, Dr. Vose for such a clear and informative presentation. As you mentioned, it is now time for the Q&A portion of the program.

We'll take the first question from the web audience. This question is from Jenny. Jenny asks, "I'm in remission now for almost four years since my autologous stem cell transplant. Should I be doing anything proactively? I've been told that CT scans are not necessary since I have other markers such as physical inflammation of nodes in the neck. Also, are there any other blood tests which might be an early detector of recurrence?"

DR. JULIE VOSE:
Thank you very much. So once you've undergone what hopefully is a curative treatment and all the scans and other tests look good after the transplant, typically we do not recommend that you have CT or PET scans or other tests like that on a regular basis, as almost always the patient comes in with signs or symptoms of lymphoma in between scans. And so it's not really been shown to be very helpful to do scans every six months or every so often to detect that. As far as blood tests, we usually do see the patient every six months or so for a few years after the treatment and then we go yearly after that, and that would be mostly for physical exam, blood tests such as CBC, chemistry profile, and that would include an LDH or lactate dehydrogenase. But again, typically the patient comes in with symptoms or enlarged lymph nodes in between being evaluated, and so it's not as helpful as one might hope it would be.

But four years after a transplant, that's really great, and the chances that the lymphoma will come back are not zero at that time, but as time goes on, less and less. And hopefully everything will continue to go well.

LAUREN BERGER:
Thank you for your question, Jenny. We'll take the next question from the telephone audience, please.

OPERATOR:
Our next question comes from Ali in California. Your line is now open.

ALI:
Thanks for taking my question. My question is, for patients who have extranodal disease, what are the standards of initial medical evaluation and then diagnosis, if you have no enlarged nodes and can't do a biopsy?

DR. JULIE VOSE:
Yes, so extranodal disease can be anywhere really. It can be in any organ or tissue. So sometimes we do do a biopsy for the initial diagnosis of that. As far as follow-up after treatment, then it would be typically CAT scans or PET scans or in some cases MRI scans, depending on the location. If it's in the bone marrow, then it would mean a bone marrow biopsy, so it kind of depends on the individual location of the lymphoma as far as what the follow-up information would be. But there's always some way to follow the lymphoma in most circumstances.

LAUREN BERGER:
Thank you for your question. We'll take the next question from the web audience and this question is from J.P. "I was told I have a very low tumor burden. My doctor told me it is treatable. I've had PTCL on a very low level for several years. Can this linger on at a treatable level without significant increase in severity?"

DR. JULIE VOSE:
There are some subtypes of T-cell lymphoma that do behave in a very indolent fashion. Most of them do not, but there are a few subtypes that do. And in some cases this can be just watched very carefully over time. And eventually usually it does come to the fact that it does need to be treated, but that may be years and years later. So each person has to be analyzed very carefully for that, with respect to the type of lymphoma, their, as you said, disease burden and location of the tumor. So I think it has to be individualized in that particular circumstance.

LAUREN BERGER:
Thank you. We'll take the next question from the web and this question is from Jane. "Are there any topical treatments or other medications that you can suggest to help relieve itching?"

DR. JULIE VOSE:
Itching is a difficult side effect sometimes to get rid of. Usually what we use would be oral Benadryl® or oral Atarax® are the two most commonly used agents. Topically typically again it would be a topical hydrocortisone or topical Benadryl. In some cases we also use antihistamines to take for medication. In addition to that, Zyrtec® or other antihistamine medications. Unfortunately, despite all those things, sometimes we just can't get rid of it. Sometimes we do have to use some pain medication or even some medications that are normally thought of antidepressants sometimes help with some itching. So it has to kind of be trial and error in each individual person.

LAUREN BERGER:
Thank you for your question, Jane. We'll take the next question from the web audience and this is from Rob and Rob asks, "Can you please talk about the status of Ontak® as a targeted therapy?"

DR. JULIE VOSE:
Yes, Ontak was a medication that had been approved in the past for mycosis fungoides or cutaneous T-cell lymphoma. And that medication had been around for a number of years and does have some good activity for those patients. It recently has been taken off the market and in the thick of things it's being reformulated. And so it has not been available for a while, but I believe will be available in the future under reformulation. So although it's not currently very available, we will have that in the future.

LAUREN BERGER:
Thank you for your question, Rob. And we'll take another question from the web and this one is from Lauren. "After having an autologous transplant five years ago for angioimmunoblastic T-cell lymphoma, my doctor is now recommending an allogeneic transplant sometime in the not too distant future. Is this common to have both types of transplant? What is the success rate of an allogeneic transplant?"

DR. JULIE VOSE:
So if the lymphoma does return after an autologous transplant, in some young people we do consider an allogeneic transplant. That's the type of transplant where we use another person's cells, not your own cells, and that type of a transplant is riskier in that we have additional complications of graft versus host disease, when your bone marrow tries to attack your body. And any time you undergo more therapy or a second transplant, it is a little bit riskier in general. And also there's increased risk of infection from that type of transplant. However, if the lymphoma has come back after the autologous transplant, that's probably one of the best options, although more risky. So you have to kind of weigh the risks and the benefits and your own personal situation to see if that's appropriate. This type of transplant, obviously we've made improvements on, but it's still a bit risky and there are patients that can actually succumb to that type of procedure. So we'd have to look at that individual person and see what the age is, what the donor is, lots of individual factors I can't really go into right now. But a consideration for sure in that circumstance.

LAUREN BERGER:
Thank you. We'll take the next question from the web audience and this one's from John. "If my disease comes back, is getting another biopsy necessary to try to understand how to best treat it?"

DR. JULIE VOSE:
It depends on probably the time interval and also the location of the tumor. If it's bit quite a bit of time or if the lymphoma is behaving differently or if, for example, a PET scan was done and there's increased activity that wasn't there before, we may consider another biopsy to make sure that it's the same type of lymphoma and it hasn't modified or changed or transformed. So it is fairly common that we do recommend that, depending on the situation, yes.

LAUREN BERGER:
Thank you for your question, John. We'll take another question from the web audience and this is from Jose and Jose asks, "Is it true that young males, treated for inflammatory bowel disease, are at risk of developing hepatosplenic T-cell lymphoma and is it because of the treatment for IBD? And if so, how can that risk be reduced?"

DR. JULIE VOSE:
It's not just young male patients, but other patients that are on some specific types of treatment for inflammatory bowel disease. Some of the treatments do suppress your immune system and for reasons we don't completely understand, that specific type of lymphoma, hepatosplenic T-cell lymphoma, has been associated with some treatments for IBD. And it could be in either a male or female patient. That type of lymphoma is quite difficult to treat and usually does require an allogeneic transplant from a donor for treatment. As far as trying to reduce the risk of developing that, no one knows for sure, but probably less time on the highly immunosuppressive medication or kind of sequencing to be on and off of that for periods of time and alternating that with other treatments may be appropriate, so again, they'd have to kind of look at that individual person to see what the risks are and to see if we can try to reduce that risk by decreasing the time on the medication as much as possible.

LAUREN BERGER:
Thank you. We'll take another question from the web audience and this one's from Matthew and Matthew asks, "What is the relationship between Epstein-Barr virus and PTCL?"

DR. JULIE VOSE:
For most patients with PTCL, there's no relationship. However, a specific type of PTCL, the angioimmunoblastic T-cell lymphoma, appears to have increased EBV associated with that in not the lymphoma cells as much, but the supportive cells in the lymph nodes and other organs. So in some cases we actually do treatment to try to get rid of some of those supportive cells with rituximab, which is an anti-CD20 monoclonal antibody, that actually gets rid of B-cells and the B-cells help the T-cells to grow. So in some forms of angioimmunoblastic T-cell lymphoma, we do use that to decrease the supportive structure for the lymphoma.

There's also another type of lymphoma that's associated with EBV and that's an NK T-cell lymphoma. And that is one that's fairly uncommon, but is associated with EBV and again sometimes we use some directed therapy against EBV for that type of lymphoma as well.

LAUREN BERGER:
Thank you for your question, Matthew. We'll take another question from the web and this one's from Carol. "I have been taking the drug Zolinza® at 400 milligrams daily for about three years, to keep the PTCL in a controlled state. What are the long-range effects of this drug?"

DR. JULIE VOSE:
Zolinza is one of the medications that was under the histone deacetylase inhibitor or HDAC inhibitor category, and there are several drugs that are under that category that do have good activity against T-cell lymphoma. That medication has now been around for quite some time, so we do have some long-term information on it. It does cause some slightly low blood counts, especially low platelet counts, so those do need to be checked on a regular basis. Need to check the liver function, make sure that those are adequate over time. And then also that classification of drugs, in a general class, does cause fatigue for patients. And so sometimes we do have to reduce the dose because of either fatigue or some low blood counts, are not uncommon.

LAUREN BERGER:
Thank you for your question, Carol. We'll take another question from the web and this question is, "What would be the best treatment for pediatric ALK-positive anaplastic large cell lymphoma?"

DR. JULIE VOSE:
Usually for the anaplastic large cell lymphoma, ALK-positive, that occurs most commonly in children or adolescents or young adults, we do recommend that they could, according to the NCCN guidelines, receive either CHOP or CHOEP as we talked about earlier. Some of the pediatric protocols are a bit more intense than that, although in the adult population it appears that those treatments are adequate. So they may be asked to be in a different protocol, but typically CHOP or CHOEP are adequate treatments for that.

LAUREN BERGER:
Thank you for your question, Mary. We'll take another question from the web and this question is from Mark and Marks asks, "Is there any relationship between sarcoidosis and PTCL and is it possible to confuse the diagnosis?"

DR. JULIE VOSE:
Where the confusion comes in sometimes is that sarcoidosis does cause enlarged lymph nodes and sarcoidosis can also cause positive PET scans. So that's why we want to make sure that we biopsy anything, to make sure that it is lymphoma versus sarcoidosis, especially if there's a history of that, because we wouldn't certainly want to treat sarcoidosis with chemotherapy. So there's no actual direct association, but we do see both in patients sometimes.

LAUREN BERGER:
Thank you for your question, Mark. We'll take another web question and this one's from Linda. "Can you explain the diagnosis of PTCL with a cytotoxic T-cell phenotype?"

DR. JULIE VOSE:
That's one of the new classifications that came out of that gene expression work that I talked about earlier. And that particular subtype of lymphoma is a little bit more difficult to treat than some of the other types of PTCL that we talked about earlier. So although we don't know the best treatment, we typically try to treat that one pretty aggressively with some high-dose chemo and probably transplantation, because we know that standard therapy does not work as well with that subtype. So a lot of information we have yet to learn by research, but we're understanding more and more every day.

LAUREN BERGER:
Thank you for the question. We'll take a question from the telephone audience, please.

OPERATOR:
Our next question comes from Cary in Michigan. Your line is now open.

CARY:
My question is, mine's stage IV peripheral T-cell. It was in the neck. Got rid of the nodules, but me and the doctor had decided just to kind of go with the flow of doing the stem cell, which I have to do with my brother. There was just a little bit of the part into the bone. My question is, does the more you wait, does it grow more into the bone and if so, is it harder to get out if I did the stem cell by waiting?

DR. JULIE VOSE:
So if the lymphoma is left there after the treatment, it is going to potentially grow back, so if you are going to consider going ahead with further treatment, I think waiting wouldn't be a great idea, if there's still lymphoma left there. So I would say that going ahead with treatment is the best idea.

LAUREN BERGER:
Thank you for your question, Cary. We'll take the next question from the web audience and this question is from Sarah. She said, "I've heard about intravenous vitamin C as an adjunct therapy on an individual basis. Do you know anything about that?"

DR. JULIE VOSE:
There's no scientific evidence that intravenous vitamin C is helpful with any type of lymphoma, so I would not recommend that.

LAUREN BERGER:
Thank you for your question, Sarah. We'll take the next question from the telephone audience, please.

OPERATOR:
The next question comes from Kathy in Michigan, your line is now open.

KATHY:
Thank you, Doctor. I was diagnosed with angioimmunoblastic T-cell in 2003. Had R-CHOP because at first they thought it was a T-cell-rich B-cell. Failed. Had an auto stem cell transplant. Failed. Was on cyclosporine that put it into remission. My question is, I've been off cyclosporine since '07, however, all my blood tests since then, it will say IgM lambda monoclonal gammopathy, IgG kappa gammopathy and oligoclonal band pattern, superimposed on a polyclonal increase in gammoglobulins, I'm just wondering, what is the significance of those three things? Is it related to the angioimmunoblastic, to an indolent or to the stem cell that I had or anything else?

DR. JULIE VOSE:
In about 1% of the population, especially as we grow older, people do have monoclonal proteins, as you've described, in the blood. And it's called MGUS or monoclonal gammopathy of uncertain significance. It is not usually associated with any other types of cancer, but it does need to be watched, so it does need to be tested on a regular basis. It's unlikely it's associated with your angioimmunoblastic lymphoma, since it's been so long, although it's not impossible. But usually we just retest that on a yearly basis to be sure it's not progressing or causing trouble. And it can develop into some other forms of blood cancer, such as multiple myeloma in a small percentage of patients, but less than 1% per year. So we kind of keep an eye on that to make sure it doesn't grow into anything.

LAUREN BERGER:
Thank you for your question. We'll take the next question from the web audience and Donna asks, "Can you please talk about the role of PUVA or light therapy in the treatment of PTCL?"

DR. JULIE VOSE:
PUVA or light therapy is typically used in some patients with mycosis fungoides or CTCL. It is not typically used for patients with the other types of peripheral T-cell lymphoma that we've been talking about today, but it is very useful for patients with mycosis fungoides and is used on an ongoing basis in some of those patients who respond to that. So depending on the certain subtype of the lymphoma, it may be quite useful.

LAUREN BERGER:
Thank you for your question, Donna. We'll take the next question from the telephone audience, please.

OPERATOR:
The next question comes from Gina in New York. Your line is now open.

GINA:
Hi. I was just wondering what types of T-cell lymphomas does the alisertib have activity with?

DR. JULIE VOSE:
Well, the clinical trial is just being finished up, so we don't have all the information on that yet, and so unfortunately I'm not going to be able to answer your question today because there really isn't enough information yet. But hopefully by the fall or next year this time we'll have further information about that.

LAUREN BERGER:
Thank you for your question. We'll take the next question from the web audience and this question is from Steve. "With autologous transplant, is the survival rate better now than it used to be?"

DR. JULIE VOSE:
Yes, that's definitely true for a number of reasons. The supportive care that we have now for patients undergoing transplant is much better than in years past. We have better antibiotics, better growth factor shots, understand how to collect the stem cells better and all those types of things really lead to better outcomes for patients. In addition we have some additional information about new chemotherapy drugs that are better for different types of lymphomas and using perhaps maintenance therapies after transplant. So by putting all that information together, yes, the outcomes definitely are better.

LAUREN BERGER:
Thank you for the question. And we'll take another question from the web and this question is from John and John says, "I'm concerned about starting to take chemotherapy. How do you feel after the first cycle of chemotherapy, what kinds of side effects and is that the same way that I'll feel after additional cycles?"

DR. JULIE VOSE:
Well, you can't compare one chemotherapy to another because they're all very different and there's hundreds of different types of therapies. So without knowing exactly what type of chemotherapy, that's going to be a little bit difficult for me to answer unfortunately. But in general most chemotherapies do make you feel somewhat tired. The other thing we always worry about are low blood counts and risk of infection, so watch out for signs of fevers or infections. I would say that probably fatigue is probably the thing that patients complain about the most. We have pretty good medications now that help with nausea and vomiting, so that's not a major issue nowadays as it was in the past.

LAUREN BERGER:
Thank you for your question. We'll take another question from the web audience and this is from Artine, "Is there a maximum number of pralatrexate cycles that can be given and is a PET/CT scan necessary after each cycle?"

DR. JULIE VOSE:
Pralatrexate in the clinical trials was given for six cycles. But there are some studies that are using it more as a maintenance therapy, perhaps at a lesser dose. So as long as the person is tolerating it fairly well and it's working, there's probably no maximum dose. PET scan would not be considered standard of care after each cycle of pralatrexate, typically we may do that intermittently, but not after each cycle.

LAUREN BERGER:
Thank you for the question. We'll take the next question from the telephone audience, please.

OPERATOR:
Our next question comes from Michele in Massachusetts. Your line is now open.

MICHELE:
Hi. Can peripheral T-cell lymphoma transform into any other type of T-cell lymphoma?

DR. JULIE VOSE:
In some cases, more of an indolent type of lymphoma that's T-cell can transform into a more aggressive type of T-cell lymphoma, but it usually doesn't transform into an entirely different type. It doesn't transform to a B-cell lymphoma, for example. But it can transform to a more aggressive type of T-cell lymphoma, so sometimes we do need to do a new biopsy or new evaluation to assess for that.

LAUREN BERGER:
Thank you for your question, Michele. We'll take the next question from the web audience. "What are the chances of relapse after being in remission following an autologous transplant?"

DR. JULIE VOSE:
That really depends on the type of lymphoma, of the time since the transplant, and a lot of other information that would have to be individualized for the person. But kind of a general quote would be that as time goes along, more and more time since the time of transplant, the relapse risk goes down with all types of lymphoma. So if a person is five years after transplant, the relapse rate would be much less than a person who's six months after transplant, for example.

LAUREN BERGER:
Thank you for the question. We'll take the next question from the telephone audience, please.

OPERATOR:
The next question comes from Ali in California. Your line is now open.

ALI:
Thanks. Could you please discuss why the peripheral T-cell lymphomas are most often diagnosed at an advanced stage, where they're already stage III or IV, and how does this compare to other lymphomas?

DR. JULIE VOSE:
So peripheral T-cell lymphoma for some reason just likes to be in some odd places. So it's more often in the skin, more often in the bone marrow, and in the organs more often. So it perhaps starts in those locations and then spreads to the lymph nodes as opposed to the other way around, as some of the other lymphomas do. So unfortunately we don't understand all that information, it may be related to some of the chemicals that the lymphoma puts off or the way that they grow and so a lot of the research is looking at that right now. The other types of lymphomas can, of course, be stage III and IV as well, but the patients with PTCL are just diagnosed at a more advanced stage.

LAUREN BERGER:
Thank you for the question. We'll take the next question from the web audience and this is from Philip who says, "My wife's main symptom, four years after autotransplant, is fatigue. Is this common and are there any recommendations to help alleviate the fatigue?"

DR. JULIE VOSE:
I would say four years after transplant, if the lymphoma is gone, under control, then the significant fatigue is pretty low. I would say 90% of people by that time would be back to pretty normal activity. So we want to make sure that there's no other reason for the fatigue, make sure the thyroid is functioning properly, the other organs and endocrine organs are functioning properly. And just look for other reasons. But most people by that time are back to pretty normal activity.

LAUREN BERGER:
Thank you for the question. We'll take the next question from the web audience and this question is from Gary. "I received an auto stem cell transplant two years ago for angioimmunoblastic TCL. I relapsed after several months. I am now starting my second year of romidepsin. I'm continuing while in remission. How does romidepsin alter outcomes in such cases?"

DR. JULIE VOSE:
Romidepsin is fairly new, so we don't have a lot of long-term information on that, but it does appear to be fairly active in patients with angioimmunoblastic T-cell lymphoma and other types of T-cell lymphoma. So as long as it's working and you're on sort of a maintenance therapy, I think that there is really nothing wrong with that, as long as you're tolerating it well. And consider staying on that indefinitely, as long as it's working.

LAUREN BERGER:
Thank you for your question. We'll take the next question from the web audience and this is from Mary. "I was diagnosed with peripheral T-cell in June, 2008, had successful chemo protocol, went mildly out of remission and then had a transplant in 2009 and I'm still in remission. Is staying in remission largely now a function of maintaining and strengthening my immune system or do you have any other suggestions to help eradicate the cancer cells or to help keep them under control?"

DR. JULIE VOSE:
Unfortunately we don't really know what we can do to try to keep it under remission, but I would say in general a good healthy lifestyle, good nutrition, exercise, all those things, help your body to be well, so

DR. JULIE VOSE:
that if the lymphoma were to come back, you can fight it better, and potentially have a better outcome. So unfortunately no specifics, but I would say just a good general healthy lifestyle is the best way to keep your health up overall.

LAUREN BERGER:
Thank you. We'll take the next question from the web audience and this one's from Scott and Scott said, "Dr. Vose, you mentioned about the importance of clinical trials. How can I find out more information about clinical trials and are there any suggestions that you can provide to me about that?"

DR. JULIE VOSE:
Sure. You definitely should ask your doctor about clinical trials. Sometimes they have some available at their center or they can refer you to one in the region, one of the larger NCI designated cancer centers, which may have clinical trials. You can also look on the web at clinicaltrials.gov, which is a website through the National Cancer Institute, that has different clinical trials for different types of lymphomas. Also through The Leukemia & Lymphoma Society, Lymphoma Research Foundation, they do have people that can help you to try to match you with clinical trials that may be close to home or even nationwide. So lots of different potential resources to look at.

LAUREN BERGER:
Thank you. And I'll just add, The Leukemia & Lymphoma Society has a specific website, which we can help you go through to help you find clinical trials that are appropriate for you, perhaps in your area, so you might not even have to travel too far.

We'll take the next question from the web audience and this one is from Sam and he asks, "Are mycosis fungoides and Sézary syndrome the same?"

DR. JULIE VOSE:
So mycosis fungoides and Sézary syndrome are within the same family of type of lymphoma. And basically Sézary syndrome is just a very advanced form of the mycosis fungoides. So it's sort of a continuum of extremes.

LAUREN BERGER:
Thank you and thank you for all of your questions. We hope that this information will assist you and your family in your next steps.

If we were not able to get to your questions, please call The Leukemia & Lymphoma Society's Information Specialists toll-free at 800-955-4572. Or reach us by email at infocenter@lls.org. Our specialists can provide you with information about lymphoma research, clinical trials and questions that you may have about treatment, specifically about PTCL, and questions about financial assistance for treatment.

Please help me thank Dr. Vose. We are so grateful she has volunteered her time with us today.

On behalf of The Leukemia & Lymphoma Society, Dr. Vose and I would like to thank you for sharing your time with us today. Good-bye and we wish you well.