WELCOME AND INTRODUCTION

Lauren Berger, MPH

[Slide 1 – Title Slide]

On behalf of The Leukemia & Lymphoma Society (LLS), **[Slide 2 – Welcome and Overview]** welcome to Case Study Discussions on the Nurse's Role in Caring for Patients With Hematologic Malignancies. I'm Lauren Berger, Senior Director of Professional Education & Engagement. The Leukemia & Lymphoma Society is committed to improving patients' quality of life through education and support, including professional education programs such as this program today. And also live and archived professional and patient web programs, for which you can earn CE (continuing education) credits. Our Information Resource Center is staffed with nurses, social workers and health educators who talk to patients, caregivers and professionals to discuss individual therapy options, including clinical trials, and to provide other disease and treatment information and support. The LLS advocates for funding to accelerate the discovery and development of blood cancer therapies and to ensure patients have insurance coverage for their care.

To date, the LLS has invested more than $1 billion in research to advance therapies and save lives. We know that you, the nurses, are treating, educating and supporting patients and that you are the key players in the day-to-day treatment and the long-term survival of patients with aggressive disease and also those living with cancer as a chronic disease. As we hear from the many patients we talk to, their nurses are the people they ask questions of to help them understand their disease and treatment issues, including questions about clinical trials. They report side effects to you, and they discuss the complexities of their care, including access to treatment, and you are there for them at every point in their care. On behalf of The Leukemia & Lymphoma Society, thank you for the very important role you play in the patient's and in the caregiver's journey.

Today, our presenters will discuss the nurse's role in caring for patients with hematologic malignancies. To receive continuing education for this program, please complete the evaluation at the end of the program, including your state and license number. A certificate of completion will be issued to you via US mail or email within 30 business days. Our special thanks to Teva Oncology for their support of this program.

[Slide 3 – Faculty Disclosures] I am pleased to introduce our presenters: Lynn Rich, nurse practitioner at JP Wilmot Cancer Center at the University of Rochester, and Beth Finley, primary nurse at Moffitt Cancer Center.

MULTIPLE MYELOMA (MM)

Beth Finley, RN, BSNc, OCN

[Slide 4 – Multiple Myeloma Case Study] Hi, everyone. My name is Beth Finley. I'm a hematology nurse at Moffitt Cancer Center, and today what I'm going to focus on is multiple myeloma, and I'm even going to put in a little bit of a case study. **[Slide 5 – Outline]** So, here is our outline. I'm going to

try and explain the disease, how we think of treatment for that newly diagnosed patient, and nursing considerations for the myeloma patient and also bringing in our multidisciplinary team to help support these patients.

[Slide 6 – What is Myeloma?] So, what is myeloma? Myeloma is a bone marrow condition. It's a malignancy of the plasma cells. **[Slide 7 – "M-Spike" – Monoclonal Paraproteins]** So, if you think of your plasma cells, their whole job in our immune system is to produce antibodies or proteins to help fight infection. Well what happens in myeloma is this plasma cell's kind of like defective and it produces this monoclonal protein, or M spike, M protein. You'll hear the terms used loosely, but it means all the same thing. This is basically their tumor marker.

So, if you take this plasma cell, as you can see from this picture, it produces that antibody. The way I explain it to patients is it's almost like a broken antibody. The most common myeloma patient is IgG (immunoglobulin G) kappa, so that becomes their tumor marker. There's also light chain myeloma patients where their protein is monitored just by the kappa or lambda, and very rarely are there non-secretors, meaning they don't even produce this M protein. We follow those patients more using bone marrow biopsy.

[Slide 8 – Diagnosing Myeloma] So, when the physician is trying to diagnose myeloma, it's like a puzzle. All the pieces have to fit. What we do is a bone marrow biopsy, and the most important part of the marrow is doing what we call FISH (fluorescence *in situ* hybridization), and that's the brains of the myeloma cell. That helps predict if it's going to behave standard risk or it's going to behave aggressively. Blood and urine tests, and when I say urine tests, I mean a 24-hour urine test. Yes, the patients will balk at that. That is not their favorite test, but it is very important, and it is needed. And imaging. We use skeletal surveys, X-rays, to determine lytic lesion. Our field is moving more and more toward PET (positron emission tomography) scans, so a PET scan is warranted as well, but typically we like the surveys, the X-rays.

So, when do you treat it? We're one of those few cancers that just because you have this M protein, it doesn't necessarily mean you treat it. So, yes, try telling the patient that we found it early, but we're not going to treat it early. **[Slide 9 – Diagnosis: "CRAB" Criteria]** When we treat is when they have some type of a CRAB (calcium, renal insufficiency, anemia and bone disease) criteria. They don't need all these. They basically just need one.

So, if you think of hypercalcemia, the myeloma cell is sending out all these cytokines to kind of break down the bone—to break up that marriage of osteoclasts and osteoblasts. So, our calcium is in our bone, you're breaking it down, the calcium leaks out, it goes in the blood and they're hypercalcemic.

Renal failure. The proteins, when they go through your kidneys—think of your kidneys like a sea that clogs it up—and it almost turns like egg white. So, their creatinine goes up. Anemia. There are plasma cells in the bone marrow. They're overcrowding the bone marrow so you can't produce your normal red cells. And fractures. Pathological fractures can happen. Ninety percent of the patients will present with bone pains, and I put infections on there (I). We don't necessarily treat, or at least in my experience, I haven't treated a patient on infections alone. They had to have another of the CRAB criteria. But, again, plasma cells are part of the immune system, so patients do get infections.

[Slide 10 – Lytic Lesions] So, here's a slide just showing some lytic lesions. I've seen it to where people describe it on the skulls, salt and pepper look, moth-eaten, but those are the lesions. When patients see them on the skull, they get pretty nervous thinking this is going to affect their brain. But the majority of those are very benign. What we worry about is the weight-bearing bones. So, you can see on the other side where it shows a picture of a humerus, and what you want to look for is a lytic lesion that is 50% or more in the cortex of the bone. They're at a high risk for a pathological fracture. We want to get the orthopedists involved very quickly on those patients.

[Slide 11 – Durie-Salmon Staging System] So if you think of our staging system, in the old days they used Durie and Salmon Staging System. It was pretty complex. As you can see, you're looking at if they're anemic, their calcium, how many lesions they have. What we found out is the majority of the patients fell in Stage III, either A or B, depending on their renal function.

[Slide 12 – International Staging System (ISS)] So, more commonly what is used now is something called the ISS (International Staging System) staging system. This helps with prognosis. It's very easy to use. You go by their serum beta-2 and their serum albumin. It makes it very simple, because you'll hear a lot of times if the patients present and they go to the ER (emergency room) and they're hypercalcemic, they think the ER physician tells them they have metastatic disease. So, our staging system isn't like the other cancers to where at Stage III it's in the lymph nodes, Stage IV is metastatic. Ours is just using this serum, and it's more prognostic features. Obviously, the best—the longest—is Stage I.

[Slide 13 – MM Risk Stratification] So, these are some of the risk factors that we look for in the bone marrow biopsy. If you remember me talking about how the FISH is the brains of the myeloma cell. This is what we're looking for. Seventy-five percent of the patients will be standard risk. They'll behave very indolent, have a good disease course. The high risk, even with all of our new therapies that are out, they still have a very aggressive course, and their prognosis is usually two to three years.

[Slide 14 – Factors Influencing Treatment Choice] So, that newly diagnosed patient comes into the clinic. What do we look for when we're thinking about treating the myeloma patient? Yes, we want to look at their staging system. What are their FISH results? Not necessarily their age so much, but what's their overall health status? How many comorbidities do they have? Also, what's their preference? Our disease is more of a chronic disease. So, for patients in the beginning, especially newly diagnosed, we use a lot of combination therapies. We do give them options. Clinical trials are our first option always. We always want to push the medical field, so research is very important for our patients.

[Slide 15 – Response Criteria] So, you're thinking about response criteria, let's say after they have induction, and I'll kind of talk about that with the case study. But when I first started working in myeloma and I saw this response, I was like, "Holy cow, there's a lot of them in there." But it's pretty simple. There's stringent complete remission. That just means there's no M protein in the blood or the urine, the free light chains are normal and their bone marrow has no abnormal plasma cells. Complete response means pretty much the same thing, except the plasma cells in the bone marrow are less than 5%.

A very good partial remission is a 90% reduction in the M protein in the blood. A partial remission is 50%. Of course, we have the MRs (minimal response) and the stable disease, which eventually as the disease course progresses, at the end of the disease, stable disease or minimal response is actually okay.

[Slide 16 – Case Study] So, let's start with our case study. Here we have a 61-year-old male. Now, I didn't mention this before, but we do see a lot of younger patients. When we are deciding on therapy with them, we have to figure out—are they working, do they have family, what's their social status? Because it's very important when we go and we talk about therapy.

So, this guy is 61 years old. He is working. He presented with anemia. He went to an outside community doctor and then got a referral to us for a second opinion. He presented with an M spike of 3.6. His IgG was around 6 grams. He had a little bit of a lambda light chain. Beta-2 was 2.3. Albumin is 3.2, therefore, making him an ISS Stage II.

His creatinine and calcium were normal. He did have a little bit of an M spike in the urine, which is about 150 milligrams per 24 hours. His bone marrow biopsy showed 70% to 80% plasma cells. He had lytic lesions on the survey. His FISH report was standard risk myeloma. So you'll see on there the 13q and the translocation 11;14.

[Slide 17 – Treatment Options for Transplant-Eligible Patient] So, when we're thinking about what treatment to offer this guy—obviously, I'm a research nurse, so we always want to think of a clinical trial. Clinical trials help push our medical field. This is how we get all these new therapies to treat myeloma. Like I've said, I'm not sure if I said it recently or not, but in the last two years, we had two new drugs approved to help treat this disease. So, we're making it a chronic disease; patients are living longer.

Unfortunately for this patient, we did not have a clinical trial available to him, so we went with our two standard of care for upfront induction therapy. The one thing I wanted to mention—this is a transplant-eligible patient, so you want to avoid melphalan with the induction. So, we started with either RVD or you'll hear it as VRD. The drugs are lenalidomide (Revlimid®), bortezomib (Velcade®) and dexamethasone. The way we give lenalidomide is every day for 14 days. Bortezomib—my physician always says day 1, 4, 8 and 11, but I really think patients don't understand that. So, the way I describe it is Monday, Thursday, Monday, Thursday and then they get a week off. Dexamethasone is 20 milligrams. They take it the day of bortezomib and the day after. The other option is what we call VDC. So, it's bortezomib—the other name of that is Velcade, by the way—Cytoxan®, or cyclophosphamide, and dexamethasone.

For this patient, he chose RVD because, again, it is a choice. We let the patients kind of help decide on what their treatment plan should be, and a bisphosphonate monthly is very important for bone health. But I'll explain that later on in the presentation.

[Slide 18 – Response: VGPR] So, this was his response. He had a VGPR (very good partial response). Whenever we see a patient, we have them go through about two cycles of therapy, and then we consult the transplant group. It takes time to transplant. You have to get insurance approval. Whenever I talk about transplant, I'm always thinking of an autologous. Very rarely do we do an

allogeneic—that means a donor cell transplant. We do, do that, but it's more in clinical trials, high-risk and younger patients.

So, this man went through an autotransplant. He saw the transplant group after a couple of cycles. He had a partial response, so a 50% reduction. They said "Give him two more cycles and then come back, and we'll be ready for transplant."

[Slide 19 – Disease Course] So, here's kind of his disease course. You can see where he started, where he responded. He got into a remission, and then he had a transplant, an autotransplant, which was very good for about a year and a half. Then, he had progressive disease. If you think about induction therapy, then they go to transplant, the average time for them to relapse is about two years. So, he had less than two years. If you think about a standard-risk patient, you would imagine that they would get maybe even a little bit better than two years. But, unfortunately, he relapsed after about a year and a half.

We offered maintenance at the time, because maintenance is still controversial in the myeloma field. We tend to do it toward the patient. We give them the option. We explain the data, and this man chose not to do maintenance with Revlimid and just monitor his bloodwork every three months until he, obviously, progressed about a year and a half.

So, as of now, just kind of an update on him: He is on Revlimid now. It's not really maintenance. Now it's treatment doses, and he's doing very well. He's actually responding.

[Slide 20 – Nursing Considerations] So, what are the nursing considerations that we think of when we think of monitoring myeloma patients? **[Slide 19 – Managing Side Effects]** First, I always think it's important to manage the side effects. This is a noncurable disease. This is a chronic disease, so we have to be good at managing their side effects because, again, if they're having a lot of side effects, they're not going to take their medication.

[Slide 21 – Immunomodulatory Drugs (IMIDS)] So, our first drug class is immunomodulatory drugs, so we call these IMiDs (immunomodulatory drugs). This is your thalidomide (Thalomid®), your lenalidomide, pomalidomide (Pomalyst®). So, I have a little box here of their main side effects. If you think of myelosuppression, lenalidomide and pomalidomide have the most with myelosuppression. So, pomalidomide can definitely make patients neutropenic. The way it's approved is for relapsed/refractory patients. The majority of these patients have already been through transplant, so their bone marrow is not as brisk as it once was before. So, depending on where they're at with their counts when you start pomalidomide, they can drop and become neutropenic. So, you just might want to keep an eye on that. I tend to monitor those types of patients weekly for bloodwork versus lenalidomide to where I do every two weeks for the first 12 weeks once they start that medication.

All these medications can cause blood clots and PEs (pulmonary embolisms), so it's very important for them to be on some type of anticoagulation. They can cause GI (gastrointestinal) side effects. Thalidomide is huge for constipation, so you always want to make sure you do stool softeners with these patients.

With lenalidomide and pomalidomide, it's more loose stools. I put on there diarrhea, but it's more loose stools, to where they tell me they eat and it just kind of goes right through them.

A rash can happen. It usually starts on their scalp. It's itchy. It can happen on their chest. We usually tell them to take an antihistamine. Anything on the face you always want to look at because there is a rare complication. It's almost like Stevens-Johnson syndrome that can happen with these IMiDs. So, you just want to keep an eye on it and make sure we look at it as nurses and assess it before we give interventions.

Sedation is huge with thalidomide, so they should absolutely take this at bedtime. We usually start them off on a low dose with thalidomide of 50 milligrams, and we work our way up, as long as they can tolerate it.

Neuropathy doesn't really happen with lenalidomide and pomalidomide. Sometimes the patients will tell me they have a little bit of numbing and tingling, but it doesn't progress. It doesn't get worse.

With thalidomide, this absolutely can happen. It happens over time, and it's almost like a sock-glove type of feel, and it is permanent. So, you definitely want to keep an eye on that, and sometimes we have to dose reduce or even take them off therapy.

All these drugs are teratogens, so whenever a patient is started on an IMiD, you have to do the black box warning. They have to promise they're not going to get anybody pregnant, which, again, this is a geriatric disease, so it kind of opens the door for lots of questions. But, in general, they just sign up for the program and they're fine.

[Slide 23 – Proteasome Inhibitors] So, moving on to our other class of medications—proteasome inhibitors. This is your bortezomib and the new kid on the block, which is carfilzomib (Kyprolis®). The way it's given, as you can see with bortezomib—I kind of talked about that previously—it's twice a week, two weeks on/one week off. The way carfilzomib is given, it's back to back. So it's more like a Monday/Tuesday, Monday/Tuesday, Monday/Tuesday and then they get a week off. Bortezomib—more and more we're using it as sub-Q (subcutaneous) because of the neuropathy. Seventy-five percent of these patients that are on bortezomib will get some grade of neuropathy, and there was a trial recently done to where if we give it sub-Q, the rate is 35%. So, we're definitely moving more towards sub-Q bortezomib. And, of course, carfilzomib is intravenous (IV).

They both can cause myelosuppression, but it's mainly thrombocytopenia. Day 8 for carfilzomib is the nadir and day 11 for bortezomib. So, it's just something you want to keep an eye on. Neuropathy—with bortezomib, it's huge. You definitely, if you're giving this medication, you want to constantly ask them about numbing and tingling, shooting, burning, aching pain. You want to keep an eye on this because sometimes we have to dose reduce.

Carfilzomib doesn't really cause neuropathy. Now, most of these patients—because of the way carfilzomib has been approved—had to have bortezomib before they can even get this medication. So, the majority of them already came with some form of neuropathy, but I have not seen that carfilzomib actually causes it in my experience.

Zoster—any patient on a proteasome inhibitor should have some type of antiviral along with it. It can reactivate that virus.

Dyspnea—definitely with carfilzomib. You've got to watch. The way it was approved as cycle one, we do it with hydration. So, you've got to be careful of giving that elderly patient too much fluid to where it kind of pushes them over the edge. So, we drop the fluids after the first cycle, and that seems to help with the dyspnea.

Fatigue is a given. These patients have been through transplant, their disease is active, and the treatment can cause fatigue. So, fatigue can happen with pretty much all of our therapies.

GI—there's not a lot of nausea and vomiting with these. I know after bortezomib, and even carfilzomib, sometimes they'll tell me they might have diarrhea the next day, but it's very well-tolerated. Again, it's quality of life. We want these patients to be able to go on their trip. So, we want to do the least amount of side effects for these patients. Very rarely there are some cardiac and pulmonary side effects with carfilzomib. But, again, it's very rare.

[Slide 24 – Steroids (Dexamethasone/Prednisone)] So here is our corporate for all the side effects. These are steroids, dexamethasone. If any of you have ever taken care of a myeloma patient, you'll notice that we sprinkle dexamethasone on everything. They cause the side effects. That newly diagnosed patient sitting in front of me gets petrified of the word chemotherapy, and I'm like, "No, no, no, no, it's steroids that cause the side effects." I listed a few. As you can see, there's mood swings, irritability, insomnia, hyperactivity, edema—the list goes on. We're very quick to dose reduce on steroids, so don't be afraid if your patient is having a lot of issues. Ask the physician. Talk to the physician about a dose reduction. It's something that we commonly do.

[Slide 25 – Nurse's Role] What is my role as a nurse? I feel like I need to educate them, support them and I did touch a little bit on my case study about how complex a regimen can be. The average age of diagnosis is 65 to 70 years. So, you have this elderly patient that came in with a whole list of comorbidities and three pages of medications, and now we're adding more medications on there. So, it's important to give these guys calendars. Write it down. Once they get past that newly diagnosed phase, they get better at understanding how we give these regimens.

We want to improve their quality of life by helping to manage side effects, whether it's from the disease or the therapy. We want to manage them to where it keeps them on therapy, and they live a good quality of life. Not quality of life of what I think. It's always what the patient thinks.

The old saying, "It takes a village to raise a child." Well, guess what, same thing with myeloma. We want to help these patients, their caregivers and their support system throughout this entire disease process.

[Slide 26 – Bone Health] Bone health is very important with our patients. They should all have bisphosphonates on board, monthly for the first two years. As a nurse, what I want to look for is invasive dental procedures. They should not have any teeth extraction or anything invasive while on a bisphosphonate. You want to hold it, let them go through the procedure. After they heal, you want to restart it. The whole idea of those X-rays in the beginning is to prevent a pathological fracture. So, if

there's a lesion that's 50% or more in the cortex of the bone, you want to get the orthopedists involved. They might need to place a rod there. Same thing with our neurosurgeon. Compression fractures are pretty common in myeloma. They have a fantastic, phenomenal procedure that helps with pain called a kyphoplasty.

All in all, pain control is very important. If you remember me saying at the beginning, 90% of newly diagnosed patients present with bone pain. So, narcotics are huge. You want to avoid NSAIDs (non-steroidal anti-inflammatory drugs). Do not take over-the-counter pain medicine. Why? NSAIDs, if you think about it, decrease the blood flow to the kidneys. Myeloma's hard on the kidneys, so we definitely want to do narcotics. Having an elderly patient take a narcotic, I understand it's difficult. Lots of education and letting them realize that the over-the-counter medication is more harmful than the narcotic.
[Slide 27 – Renal Health] Renal health. These patients can get renal failure very quickly. Hypercalcemia, dehydration, CT (computerized tomography) scan dye, IV CT scan dye—you want to avoid that—NSAIDs, some of our antibiotics, gentamycin, tobramycin and even bisphosphonates. We think it's more how fast you infuse the bisphosphonates that can harm the kidneys. But you want to make sure they're drinking and they're staying hydrated.

[Slide 28 – Anemia] Anemia can be caused by the disease and the treatment, so we want to support them. Again, it's quality of life. If they're short of breath, they're not moving around, they're tired, give them a blood transfusion or maybe they even need erythropoietin-stimulating agents. Fatigue is a vicious cycle. It can happen because of anemia, treatment, lack of exercise, **[Slide 29 – Safety and Mobility]** so it's something definitely we want to get our physical therapy, our occupational therapist involved.

Nutrition and hydration—very important. If you ask a geriatric patient how much they're drinking, it's usually a cup of coffee in the morning and a little bit of sweet tea for dinner. So, you want to make sure they are hydrated and explain it to them. How much hydration do they need?

Their psychosocial well-being. How's their support system? Sleep disturbances—is this because they have anxiety/stress? Is it financial stress? Is it the dexamethasone? **[Slide 30 – Multidisciplinary Team Approach]** So, this is something you want to keep in the back of your mind to always talk about with the patients. You want to get the multidisciplinary team approach. You want to get all of our social workers involved. I already mentioned the physical therapist, the dietitian, the pharmacist. It's a village to support these patients.

There are lots of financial assistance programs out there. We're very blessed to have The Leukemia & Lymphoma Society help our patients. There's Chronic Disease Fund, Patient Network Access. Even the pharmaceutical companies help these patients find programs to help pay their copays for therapy.

[Slide 31 – Summary] So, in short, multiple myeloma is a chronic but a very treatable disease. We have lots of new drugs. We've had two approved in the last two years. We have a few more that we're hoping to be approved this year. So, we're making patients live longer. Treatment decisions are individualized. We always take into consideration the patient, their support system. Are they working? Are they not working? We want to manage their side effects. We want to help them maintain their

quality of life. As always, let's get our other team involved. Let's get the social workers, the physical therapists, the dietitian. Let's get everybody involved and help support these patients and their caregivers.

[Slide 32 – Thank You] So, at this time I wanted to thank The Leukemia & Lymphoma Society for all their support for our patients, our nurses, our healthcare providers by providing financial assistance, education materials that are on the Web, in booklets, through chapters across the country.

As a nurse, I am very appreciative of the professional education programs bringing the newest information and understanding of the hematological diseases. So, thank you again to The Leukemia & Lymphoma Society.

FOLLICULAR LYMPHOMA (FL)

Lynn Rich, ANP-BC, OCN

[Slide 33 – Follicular Lymphoma: Case Study] Good afternoon. My name is Lynn Rich. I'm a nurse practitioner from Upstate New York in Rochester. Today, I'm going to talk to you about follicular lymphoma, and, most specifically, we'll try to embrace a case study to help better understand the disease.

[Slide 34 – Outline] Here's an outline, and we will essentially define the disease; talk a little bit about epidemiology, how often is this occurring; take a look at the natural history of the disease, the fact that it's indolent versus curable; approved treatment options, including rituximab (Rituxan®) maintenance versus observation; use of idelalisib (Zydelig®); and different communication strategies using support of social workers. At the very end, we'll explore some resources in survivorship challenges.

[Slide 35 – Lymphoma] So, just to start off, let's take a look at what lymphoma is. It's the general name given to a group of cancers that affect the lymphatic system. It includes the lymph nodes, plasma cells, spleen, lymphatic vessels and bone marrow, including immunoglobulins. Remember, it's the immune system that helps protect against disease and infection. So, a dysfunction in the immune system is kind of what brings lymphoma.

[Slide 36 – Lymphoma] Lymphoma is broken up into non-Hodgkin's and Hodgkin's lymphoma. There are at least 50 different subtypes of non-Hodgkin's lymphoma. Hodgkin's lymphoma has only approximately five different subtypes.

[Slide 37 – Follicular Lymphoma] Follicular lymphoma is thought of as a B-cell, non-Hodgkin's lymphoma versus T cells. It is damage to DNA of one of the parent B cells that causes a malignant transformation, resulting in uncontrolled and exaggerated growth of the lymphocyte. As you can see here, these are the hematopoietic stem cells that initially produce. As they progress down the line and develop, we can see that the more mature cells are the dysfunctional ones in the hematopoietic system.

[Slide 38 – Follicular Lymphoma] Follicular lymphoma is the second most common subtype of non-Hodgkin's lymphoma. The average age at diagnosis is 60 years old. It's thought of as an indolent or very slow-growing disease. It's treatable, but not curable. What we mean by that is, when treatment is necessary, we use a list of arsenals which help guide us as far as our future treatments.

[Slide 39 – NHL: Epidemiology] Epidemiologically, how many times does this occur for non-Hodgkin's lymphoma? Seventy thousand new cases occurred in 2014. As you can see, the bright orange is the diffuse large B cell. It's the number one most common lymphoma. The second is the blue piece of pie, and it's showing that follicular lymphoma being the second most common. T cell is less common, and the pink is all the different lymphomas. As I said, there was 50+. So, take out the top two, and there's all the rest of the different lymphomas—mantle cell, marginal zone, all the multiple different kinds of lymphomas that are occurring.

[Slide 40 – Case Study: MB] So, what we thought we would do is bring in a case study, because that always helps us better understand a specific disease. What I am presenting to you is a patient of mine. Her name is Martha, and she is a 57-year-old married female. She's a third-grade elementary teacher. She essentially presented with abdominal fullness; sweats, which we described those as sweats occurring cyclically, mostly every night around the same time, causing one to change her pajamas and sheets because the sweats are so significant. So, it's different than a menopausal, "Oh, I felt hot. I felt sweaty." This is cyclical. They can describe to you sweating of sheets, changing pajamas and them occurring cyclically at the same time.

Next is fatigue. It's very, very common. We see that in a lot of our world. But this fatigue is quality of life limiting. It's changing their daily behavior. It's impacting everything they're doing.

[Slide 41 – Ann Arbor Staging System] Finally, lymphadenopathy—multiple sites of lymph nodes throughout the body. By that, we have to better understand and stage a patient with follicular lymphoma. When we stage in follicular lymphoma, we have a very specific staging system. It's called the Ann Arbor Staging System. Stage I is described as one isolated site of disease. Stage II occurs when there are two sites of disease that are occurring both above the diaphragm or both below the diaphragm, so either or, versus Stage III which is above and below the diaphragm. A Stage IV is above and below the diaphragm, including organs or bone marrow involvement. So, a Stage IV will be declared by either non-nodals, organ, or bone marrow involvement.

[Slide 42 – Case Study: MB] So, when we first meet someone, we do CT scans and that better allows us to identify what stage they're in. Our patient, Martha, was noted to be a Stage III, and by that we noticed she had bilateral axillary. So, she had lymph nodes under both arms. They were small, but they were there. Secondly, she had a very large abdominal mass. It was ten centimeters, and she is quite thin and petite; we were actually able to feel that, so that was really how she presented with that full abdominal fullness. Secondly, she had a small inguinal or a groin node. She did not have bone marrow involvement, so that kept her at a Stage III. You note above and below the diaphragm there were no organs involved, and the bone marrow was negative. So, again, she was a Stage III.

[Slide 43 – Treatment] So, when we first meet someone, we have to explain to them that we're on a marathon. We're going to treat you when we have to. For as long as we can, we're going to try to not treat someone. If they don't need treatment, that's great. Then, we continue to follow them. Oftentimes we meet them at an earlier stage, and we can watch their disease. Treating them early does not help their prognosis. Remember, it's a marathon. We're going to treat, put them in remission. Treat, put them in remission. The longer they go in between each chemotherapy regimen, the longer their survival lifespan is. So, we do what we call watch and wait; now, actually, we're trying to describe it as a time of observation. So, it's not necessarily watching and waiting. We are observing them and we're actively observing. It's a kind of attempt to try to get patients to not be so intimidated by that idea. It's very scary to say, "What do you mean I have cancer? What do you mean you're not going to do anything? What do you mean we're going to watch it?" So, we describe it as actively observing until the time comes when we actually need to treat.

Just to better understand, we stage to I to IV, but follicular lymphoma is also described as either a Grade 1, which is very slow growing; a Grade 2, moderately growing; or Grade 3, which is

aggressively growing cells under the microscope. So, not only do we stage somebody, we stage them with what grade their actual lymphoma is, and that's found by the pathologist under a microscope guiding us about what grade they're at.

[Slide 44 – Ready to Treat] When we actually decide about whether or not somebody is ready to treat, because, remember, our goal is to not treat. We want to have them live as long as we can without actively coming in with treatment.

So, in follicular lymphoma, the criteria guide us about when or whether or not we need to treat, such as if there are more than three sites of disease, three centimeters or more. Number two, if one node measures seven centimeters or more. Cytopenias, refractory thrombocytopenia disease. So, they have low counts, and they're not recovering. They're lingering, they're low—that's potentially causing them trouble. Whether or not they have effusions and whether or not they have symptoms of disease or B symptoms. That's what I described earlier—night sweats, fevers, weight loss. If they're having any of those, that will actually impact whether or not we're ready to treat. Finally, if they have threatened organ involvement or an elevated LDH (lactate dehydrogenase).

So, in our patient's case, she was ready to treat. We can see that just by the number two—one node measuring seven centimeters. She had that. She had a ten-centimeter node. She actually had B symptoms, and she had more than three sites of disease. So, she clearly fits criteria and is ready to proceed with treatment.

[Slide 45 – Case Study: MB] So, in her case, we treated her with R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone)—that's the old standby. It's what we've been using for years and years in lymphoma. She underwent this in 2007. She attained a complete remission, which is most expected with follicular lymphoma. Patients typically will respond to disease. It's just a matter of how long their remission will last.

Secondly, we'll consider maintenance with rituximab versus observation. Now back in '07, that wasn't an option. We were not doing maintenance therapy. That has become a little bit more in fashion, and there are different criteria. Whether we do maintenance Rituxan® (rituximab) is a decision if it's upfront versus consolidation, meaning, in her case, it would be to consolidate, to complete therapy, and to try to contain the remission. We considered the expected response, the impact on overall survival, quality of life and financial impact. So, maintenance Rituxan is often thought of as a lot of considerations that providers will discuss with them about whether or not they want to proceed with that.

[Slide 46 – Case Study: MB] In Martha's case, we did not do maintenance rituximab. That was not standard of care back then. It wasn't something that was considered. It's much more upfront therapy, considered consolidative therapy with upfront in this year, 2015.

So, she actually relapsed in May of 2008, so she only got a year. So, that's not very long. The typical time until relapse with upfront R-CHOP therapy for follicular lymphoma is three to five years. She relapsed in only one year, so that was pretty concerning. That's an indicator that her disease was behaving more aggressively, and it was more the Grade 3. She responded but the disease came back rather quickly.

So, in 2008, the treatment of choice was to proceed with an autologous stem cell transplant, which she did. She was still young—less than 65 years old. We felt she could tolerate this quite well. She underwent salvage therapy, which is a chemotherapy regimen to get her ready for the autologous transplant. She underwent two cycles. She did very well. She did the autologous transplant and obtained a complete remission in September of 2008. So, she did well with that, and happily it put her in remission.

[Slide 47 – Case Study: MB] Unfortunately, she relapsed in 2014, but that's pretty good. She went six years off the autologous transplant. She did well. Now, we're basically in December of last year. She was essentially asymptomatic, but she did experience some mild abdominal fullness. We rescanned her, which is pretty typical to take a peek since she did experience this fullness. There was concern there could have shown some disease progression. She had the CT of the abdomen, and it showed an increase in disease. So, now at this point, is she ready for treatment? Now, we're wondering "What are her treatment options?"

Multiple chemotherapies—we can certainly consider that.**[Slide 48 – Idelalisib – What Is It?]** But now we have an exciting new option called a PI3K (phosphoinositide 3-kinase) inhibitor, otherwise known as idelalisib. Now, a PI3K inhibitor is a really relatively new mode of treating lymphoma. If we think about what that is, we understand that, in order for a lymphoma to grow, there is a multiple molecular chain that must progress from one's chain reaction from one molecule to the next. A PI3K is what they identify as one of those specific molecules that they know is necessary for lymphoma to grow. So, this inhibitor, just as it describes, inhibits the PI3K to actually move from one chain to the next, so it stops the flow of this molecular chain reaction and the lymphoma can no longer grow.

[Slide 49 – Idelalisib] So, the drug we describe is idelalisib, and it's an oral agent which is exciting. Most of these patients have seen multiple different chemotherapy infusional treatments. It's a pill, so it's pretty well tolerated. It's FDA (US Food and Drug Administration) approved in 2014, so just last year. It has become available to any patient who has relapsed follicular lymphoma.

So, not in the upfront, meaning if you're newly diagnosed and you have disease, idelalisib is not available for you at that point. It becomes a choice if one has relapsed disease. It's also used in CLL/SLL (chronic lymphocytic leukemia/small lymphocytic lymphoma). So, it's an exciting new option, and patients are pretty excited about it because it's essentially very well-tolerated. **[Slide 50 – Side Effect Profile]** There are a few side effects that are important to understand with patients using this drug. There's a concern for pneumonitis. So, what we mean by that is they have cough, shortness of breath and it's a new change in their quality of life and in their breathing. So, when one comes in with new shortness of breath—it's actually quite subtle when it first presents—but it's important to stay attuned to that because if a pneumonitis develops, it can actually make you quite ill, quite quickly, oxygen-dependent and requiring steroids. It's very important to stop the drug and resolve the pneumonitis in order to move forward.

Secondly, there's colitis. So, in general, patients do quite well for a few weeks to a month. But after some time, four to six weeks, they slowly may develop episodes of diarrhea in one or two, three a day tolerable, every other day, something we're not particularly concerned about. But if it progresses and they're occurring three to five times per day for multiple days on end, clearly that's a sign of

intolerability and the drug must be stopped. It can develop and become a true oncologic emergency if it progresses without stopping disease. Finally, there's concern for an evolution of liver function abnormalities in general. What I mean is the LFTs (liver function tests) will spike, and it usually doesn't occur until at least four to six weeks once on the drug. You typically see normal functions, normal function and it can spike right up.

So, actually, with our patient Martha, we actually saw that. She tolerated the drug quite well. Four to six weeks into it, she was doing well. At the six-week point, her LFTs, out of the blue, were spiked to four to five times normal liver function. So, we actually had to stop the drug. If you don't stop, they can become quite ill, and yet again it's an oncologic emergency. So, we stopped the drug. Over time you'll see it slowly work its way down, and she actually did slowly work itself down. It's taking at least eight weeks, which is pretty common from what I understand. Six to 12 weeks is very reasonable for LFTs to recover.

Once they do recover, we want to restart the medication but at a lower dose. So, there's a 75% chance that patients will attain normal LFTs. Once that happens, you can restart the medication. However, it's at the lower dose. So, a standard dose is 150 milligrams BID (twice a day), and the new dose, if one needs to get restarted on medication, is 100 milligrams BID. So, typically once they go to the lower dose, it's better tolerated, and we no longer see those elevated LFTs.

[Slide 51 – Things to Consider] So, when we think about patients with relapsed follicular lymphoma and we're excited about trying one of these new agents, it's important to decide whether or not this patient is a good candidate. We get all excited. Oh, it's just a pill, twice a day. It could be somewhat challenging in your gerontological population. Fortunately, she was 57 years old—she's still pretty spunky. She was a school teacher. She's incredibly anal and attentive to details. She writes out calendars. She knows exactly what she's doing with her doses, so it's very easy. She is an excellent candidate actually to undergo oral agents at home.

However, if one is not the case, I think it's important to bring in the social worker. They'll help you assess the medical literacy and the implications. If they're old, they don't understand the language, it could potentially be quite difficult for patients to manage. So, it's important to make sure they are in a receiving end to be able to tolerate the instructions and follow through on what they're supposed to.

Secondly, there's financial assistance. This is an incredibly expensive drug. Fortunately with the FDA approval, it's covered by insurance if it's in the relapsed setting. But even in those cases, it's still somewhat concerning, so we think about what are the potential sources of assistance. Happily, The Leukemia & Lymphoma Society is very supportive and helpful, and we very much appreciate their impact in allowing our patients to get the medications they need.

I talked a little bit a minute ago about whether or not they're good candidates. I think just to really specify—are the patients able to follow instructions? We often suggest, as nurses, our role is to help them make sure they better understand what they're supposed to do. **[Slide 52 – Communication Strategies]** We often suggest creating a calendar, when to take the pills, when to get their blood drawn and how to follow up if there are issues.

So, we talk to patients. We talk to them regularly on the phone, consider MyChart®, which is our lingo for being able to email patients and respond to them over the computer. It's been quite helpful.

Eventually, patients will evolve to monthly visits if it's well-tolerated. **[Slide 53 – What Happened to MB?]** What happened to Martha? She began idelalisib at 150 milligrams BID. She did quite well. She had no issues. She felt well. She didn't experience nausea. It's a very well-tolerated drug. It typically does not cause nausea.

She tolerated 150 milligrams twice a day up to six weeks; around eight weeks, again , she actually had escalated LFTs, so we had to stop the drug. To date, actually, she's still off the drug. But it's only been, at this point, eight to ten weeks. We have seen them come back to almost normal. Now, at this point though, only two times normal as opposed to four to five times normal. So, she's working her way back to normal LFTs, and we expect her to be able to get back on the drug.

[Slide 54 – Resources – Survivorship Issues] Finally, as I mentioned earlier, there's a little bit of importance to make sure we recognize the different resources. These are survivors. Patients with follicular lymphoma will live many, many years. It's important to make sure we offer them all the resources we have. The Leukemia & Lymphoma Society is a fabulous resource. We have local chapters. They support our patients regularly. We also can suggest the YMCA. There's an exercise program which is really important for patients to maintain normal health, and fitness really ultimately helps with their ability to cope with their survivorship. We also make it an important goal to make sure all of these patients have survivorship care plans.

[Slide 55 – Thank You] Thank you to The Leukemia & Lymphoma Society for supporting patients by providing financial assistance, educational materials on the Web, in booklets and through LLS chapters across the country.

As a nurse, I also appreciate the professional educational programs bringing the newest information and understanding hematologic diseases.