TRANSCRIPT
Building Nursing Knowledge Through Case Studies:
Clinical Trials, Genomics and Prognosis
May 3, 2014

Slide 1: Building Nursing Knowledge Through Case Studies
Lauren Berger:

Good afternoon and welcome to *Building Nursing Knowledge Through Case Studies: Clinical Trials, Genomics and Prognosis.* I'm Lauren Berger, Senior Director, Patient and Professional Education, at The Leukemia & Lymphoma Society.

The Leukemia & Lymphoma Society exists to find cures and ensure access to treatment for blood cancer patients. Our vision is a world without blood cancer.

Slide 2: ONS Disclaimer

For more than 60 years LLS has helped to pioneer innovations such as targeted therapies and immunotherapies that have improved survival rates and improved quality of life for many blood cancer patients. To date, we have invested more than $1 billion in research to advance therapies and save lives. And advances are far-reaching. From 2000 to 2013, almost 40% of new anti-cancer drugs were FDA approved for blood cancer patients, more first-ever approvals than for any other group of cancers. And many of these were advanced with funding from The Leukemia & Lymphoma Society.

Slide 3: Welcome & Introductions

We are the leading source of free blood cancer information, education and support for patients, survivors, families and healthcare professionals. And we touch patients and communities through our 61 chapters across the United States and in Canada. And also via national education programs and support programs, such as this program today.

I hope you will use the link in the back of your workbook to access information on patient education, professional education and other support services for yourselves and to share them with your patients.

Our Copay Assistance Program helps eligible blood cancer patients afford health insurance premiums and prescription drug copays.

I am now pleased to welcome Christine Magnus-Moore, board member from the California Southland chapter of The Leukemia & Lymphoma Society. Christine?

Christine Magnus-Moore:

Hello, oncology nurses. On behalf of the California Southland chapter of The Leukemia & Lymphoma Society, I'd like to welcome you to Anaheim and to our symposium today. I am so happy to be in the midst of you extraordinary nurses.

The majority of my nursing background has been in oncology, primarily adult and pediatric bone marrow transplant. I have also worked as a bone marrow transplant

coordinator, general oncology nurse, ER and recovery room. Oncology patients have always held a special place in my heart. I am a non-Hodgkin lymphoma survivor of almost 12 years. Thank you. Thank you.

I just finished writing a book called *Both Sides of the Bedside*, which is about the perspectives and dichotomy of what it's like being an oncology nurse and a cancer patient.

I am truly honored to be a board member for The Leukemia & Lymphoma Society. LLS has so much to offer. From endurance events called Team in Training, which raises funds to help support blood cancer research clinical trials, to the First Connections program, offering one-on-one patient-to-survivor connections, LLS's main goal is to serve blood cancer patients.

I've been a Team in Training participant and just completed my third half marathon. Thank you. I am also a First Connections volunteer and have had the privilege to be matched with numerous newly diagnosed patients, helping offer them comfort in knowing someone else has walked through the cancer journey.

If you are not already connected with the LLS chapter in your community, use the web links and telephone numbers on the inside cover of your workbook to access education and support resources for you and for your patients.

I hope the information presented, as well as our discussions in this session, will provide an interesting and valuable learning opportunity. And I am happy to learn with you.

Lauren Berger:

Thank you, Christine.

During today's symposium our presenters, Amy Goodrich and Donelle Rizzuto, will discuss the role of nurses in educating, helping to enroll and in treating patients in clinical trials, how genomics research relates to treatment and prognosis for patients with blood cancer, how diversity issues impact patients as they make decisions, and also impacts communication with the patients. Strategies for nurses to communicate about genomics and clinical trials will be discussed. As well as how to address the ethical issues that you may encounter in caring for patients.

We encourage you to share thoughts and best practices during small group discussions that will be built into each of the presentations, allowing you for time to talk with each other. And also we hope you'll ask questions of the speakers during the Q&A session. Helping to make this an interactive session will allow you to bring back information to your patients as well as to share ideas and things that you've learned over the years with the colleagues that you're sitting with today.

Thank you to our esteemed speakers and to all of you for sharing your time with us today.

Please silence your cell phones and other electronic devices.

Refer to the learning objectives in your workbooks and also the information for full disclosure.

To receive continuing education credit, please complete the evaluation in the back of your workbook before you leave today and hand it to the staff at the end.

For continuing education credit throughout the year, The Leukemia & Lymphoma Society offers free CEs. They're online and we provide information at the back of your workbook, as well as through our chapters throughout the country.

So I hope you will find this a very valuable learning experience and I'll now turn the podium over to Amy.

Slide 4: Non-Hodgkin Lymphoma
Amy Goodrich:

Good afternoon and thanks for coming. I'm Amy Goodrich. I'm a nurse practitioner from Johns Hopkins in Baltimore. I am going to talk to you about non-Hodgkin lymphomas. And hopefully all of you will come out of here with a little more information about how to provide the best care you can for your patients.

Slide 5: Non-Hodgkin Lymphoma Incidence

So just to sort of get everybody on the same page. Non-Hodgkin lymphomas, as you know, are not all created equally. There are many types with different prognosis, treated differently. They're not all the same beast. About 70,000 people in this country will be diagnosed this year with non-Hodgkin's lymphoma. It goes back and forth between being the sixth and seventh most commonly diagnosed malignancy. And almost 20,000 people will die of non-Hodgkin's lymphoma this year.

Slide 6: Frequency of NHL Subtypes

So the frequency of the subtypes. Sometimes non-Hodgkin's lymphomas are really hard to get your heads around because there are so many subtypes. This pie shows really mainly the most common ones. As you can see, diffuse large B-cell is the most commonly diagnosed lymphoma in the United States.

Slide 7: Risk Factors Associated with NHL

Risk factors. So who gets lymphoma? So children get lymphomas, as you all know, but lymphoma is really a disease of the aging. So the older you are, the higher the likelihood is that you will develop a non-Hodgkin's lymphoma. Folks with immunodeficiency disorders, AIDS. Folks on chronic immunosuppression for organ transplants. Folks with autoimmune disorders. There are some lymphomas associated with infectious etiologies such as HTLV-1s, EBV, H. pylori. And then environmental exposures, drugs, chemicals, occupational. I think of the lymphoma belt, which is the Midwest, where all of the chemicals and the pesticides and the things that farmers use cause a higher incidence of lymphomas. Our Agent Orange military folks, that's one of the indications for benefits. But really the average patient will have none of these. So it's not always clear why your patients are developing lymphomas.

Slide 8: Ann Arbor Staging System

So staging. Just to get everybody on the same page, too. Staging is Stage I is one lymph node or one lymph node chain. Stage II is more than one, but on the same side of the diaphragm. Stage III is both sides of the diaphragm. And then Stage IV is disseminated, and for most patients that's bone marrow involvement. And you might see

an E for extranodal. You might see A and B for symptoms. A is no symptoms. B is fevers, night sweats or weight loss. And then there's this newer one that's X for bulky, meaning any node greater than 10 centimeters. So that's staging.

Slide 9: What's New in NHL?

So I want to start with what's new in non-Hodgkin's lymphoma. And as Lauren eluded to, there's a lot new in hematologic malignancies, but there's a lot new in non-Hodgkin's lymphomas.

Slide 10: Ibrutinib

So by a show of hands, who's heard of ibrutinib? Love it, okay, great.

So ibrutinib was FDA approved in November of last year for use in relapsed/ refractory mantle cell. And then was approved just in February, a few months ago, for use in second line or further in CLL. So it's first-in-class. It's a Bruton's tyrosine kinase inhibitor and it's the first one on the market. Certainly not the first one being studied. Will not be the last. But is the first one. So tyrosine kinase inhibitors, they move phosphate and phosphate functions as an "on-off" switch for cells. So when there's a lot of phosphate going into cells, they grow very quickly, so all these tyrosine kinase inhibitors turn that phosphate off. It's really just like a light switch. Even though sometimes you see these slides that are very complex and really hard to grasp, it's all about turning a light switch on or off. So these are great drugs. You know you're giving these kinase inhibitors to lots of patients. But now we've got really good ones for lymphoma.

Slide 11: Ibrutinib Pivotal Trial in MCL

So I just wanted to talk to you about the mantle cell trial. There were 111 patients and they were spliced out into two groups. The folks who designed this trial really thought that patients who had been exposed to bortezomib would have a different toxicity profile or different response rate than those who had not been exposed, either at all or very low dose – just a little bit of bortezomib. So they looked at those folks differently. The median age was 68, so these were not cream of the crop patients. Most of them had unfavorable disease. Again, not cream of the crop. Most of them had had three prior therapies. Thirty percent had hyper-CVAD, which all of you know is a pretty nasty regimen. And over 10% had had transplants. So again, these were pretty beat up patients.

They all got 560 milligrams a day. And like many of our oral drugs now, stayed on until progression or unacceptable toxicity, which is definitely the wave of our drugs now in oncology, versus our cycle-based approach even ten or fifteen years ago.

Slide 12: Ibrutinib Pivotal Trial in MCL

So in looking at side effects, you can see that this is a pretty typical side effect profile. Some count issues, diarrhea, constipation, things like that. The middle aisle is Grade 1 and 2. And I'm terrible with left and right. As you're going across the far column is Grade 3 and 5 toxicities. So if you look at this, 16% of patients developed a neutrophil count under 1,000. Only 11 – is that 11? I can't see. You hit 40 and you can't see any

more. So 11% developed a platelet count less than 50,000, which, you know, are all reasonable, those are pretty low numbers compared to some of the chemotherapy regimens that we give to these patients. So if you look at nausea and vomiting, none of them had severe nausea or vomiting. None of them had severe constipation. So this is really a very reasonable side effect profile.

Slide 13: Ibrutinib Pivotal Trial in MCL

So what happened to these people? So 7% had to come off due to toxicity. Which is a pretty low number. Fourteen percent died. And you can see there, 12 of the 16 died of disease progression. So that sort of makes me feel better that if it didn't work, it didn't work, and that happens. But toxicity-wise, two pneumonias, one sepsis, and one unrelated MI. So there were no toxicity differences in the two groups, the bortezomib or the non-bortezomib folks. And at 15 months followup, the response rate is 68%. Now remember these are mantle cell patients, average of three prior therapies, so pretty beat up patients. The estimated duration of response is almost a year and a half, which is a great, great response rate for these patients. And then the estimated overall survival is about 60% at 18 months.

So a great side effect profile. Not a lot of toxicity. It's a pill. Great responses for these patients.

Slide 14: Obinutuzumab

So obinutuzumab. By a show of hands, who's given obinutuzumab or heard of obinutuzumab? Okay, so not quite as many, which is not surprising. But let me tell you about this drug.

Obinutuzumab is a fully humanized anti-CD20 monoclonal antibody. It was approved for use in November of 2013 in CLL, untreated CLL, with chlorambucil. And so I'm assuming that most of you have not given it or heard of it because we are not, in the United States, big chlorambucil fans. So compared to rituximab, it produces more antibody-dependent cell-mediated cytotoxicity, so harnesses the immune system a little more effectively than rituximab does, in the lab. And superior cell death directly from the drug.

Okay, so is this going to be a rituximab replacement? Who knows? But for those of you involved in clinical trials or having patients on clinical trials, you're going to see this going head-to-head with rituximab in just about every setting that you can imagine. So if you have not heard of it and have not given it, it'll be a very short time until this is in your clinical area, like wildfire.

Slide 15: Obinutuzumab Pivotal Trial in CLL

So this got approved through a European trial. And in Europe they are much bigger chlorambucil fans for initial therapy in CLL than we are. So chlorambucil is the standard of care in Europe. So what they did was they took almost 800 patients with untreated CLL and a high risk feature, meaning lots of coexisting medical conditions, renal dysfunction. So patients who you would really not want to give systemic therapy to. So these are clearly not the cream of the crop here.

So the median age was 73. And it was a three-armed randomization. They either

got chlorambucil alone, which is the standard of care in Europe for folks like this; they got chlorambucil with obinutuzumab; or they got chlorambucil with rituximab. Okay?

Slide 16: Obinutuzumab Pivotal Trial

So let's look at response rates. So the chlorambucil alone, overall response rate of about 32%. So this is why in the United States we're not fantastic chlorambucil fans. Almost no complete response rate. With obinutuzumab and chlorambucil, the response rate went up to almost 80%. And about 20% complete responses. And then if you look at the rituximab-chlorambucil arm, their overall response rate was 65%. Only 7% complete remissions. So clearly adding the obinutuzumab to the chlorambucil did a better job than the rituximab. And heads and shoulders better than chlorambucil alone.

Slide 17: Obinutuzumab Pivotal Trial: O + C Arm Only

So in looking at side effects of this superior arm, infusion reactions are really the biggest issue with obinutuzumab. And I'm going to show you a slide on how the obinutuzumab is given, because I promise you you're going to be giving this. Neutropenia is an issue. Infections are an issue. But again, they got this with chlorambucil. So don't forget that there was an oral chemo drug being given. But really in general, other than the infusion reactions and the count issues, this is a well tolerated regimen.

Slide 18: Obinutuzumab Pivotal Trial in CLL

So how is obinutuzumab given? And this is kind of a busy slide. But the bottom line is it's given on the first cycle, day 1, 2, 8 and 15. Then it's given once a cycle like you're giving your rituximab. So if you look at this, day 1 cycle 1, folks get 100 milligram flat dose over four hours with no escalation. Pre-medded with acetaminophen, an antihistamine, usually Benadryl. Everybody gets a steroid. So this is different because you're not automatically pre-medding all your rituximab patients with steroids. So they get a little dose over four hours with lots of premeds.

The second day they come back and they get 900 milligrams. It's given just the way you give a first dose of rituximab. But they also get all those premeds again. So it is different.

Day 8 they get the full 1,000. Escalated just like you would do a second rituximab. So there are some similarities, but there are lots of differences, too. And again, what you're doing with premeds depends how the patient did with their first two doses. So the goal is eventually you get them down to just the acetaminophen, but you do it at the rate that the patient tolerates it.

And then when they get subsequent doses after the first cycle, it's just on day 1 only. And again, it's premeds based on how the patient did with the previous doses. Whereas with rituximab, you're basically giving the Tylenol and Benadryl every time. You're going to be doing it differently with these folks, based on how they tolerated it.

So just get ready for this to come. If you lose these slides, it's in the package insert, so you can find this somewhere else. But just know that there are lots of similarities, but lots of differences, too.

Slide 19: Discussion Question

So before I move to my case study, this is where in your tables we need you to start talking about these questions.

So I'm going to move on to my case study where there were some ethnicity issues – or not issues, but just angles. So in your practice, how do a patient's age, race and ethnicity impact treatment decisions and also how you educate your patients? And how do those differ for patients receiving standard of therapy versus those being approached with clinical trial options?

So if you can just within your tables, talk about that for a few minutes. And if somebody's got a real doozy, we need a couple of tables to come to the mics that are – I see one here and I see one over there – to come and volunteer to tell us your story or give us an example of a memorable patient.

Audience:

Something that we discussed at our table was education when it comes to standard therapy versus clinical trials. Patients will ask questions like the clinical trial, a lot of questions, and my answer is, "I'll go check with the pharmacist and get back to you." So sometimes it's hard to be able to feel like you're an expert on something when you're not an expert on something.

Amy Goodrich:

Got it. Got it, that's a good point, too. How many of you have patients, just by a show of hand, who are on clinical trials? And how many see the same trial or trials over and over again, that you can become comfortable talking to patients about them? Okay, so a smaller group of you, but yeah, I think that is definitely a challenge for those of you who see lots of patients, lots of diseases, lots of trials.

Audience:

So I actually did have a situation about a month and a half ago. We had an elderly female Vietnamese patient. She was 82. Had lymphoma and unable to make decisions for herself. And even within her culture, it's acceptable for the family to make the decision for proceeding with treatment. She had ten children. And her husband, also his mentation was not there, so he wasn't really able to help with that decision-making process. So it was very difficult because the children did not all agree on, you know, if we're going to proceed with treatment, if we're not going to proceed with treatment. We had to get an ethics consult involved. It was not acceptable within their culture to tell her that she had cancer. Which I'm sure many of you have encountered. Also makes it complicated when you have to do the consent for chemo, which we did end up proceeding with. Because how are you supposed to sit there and say, okay, we're going to start this drug and we're going to do this and that and you can't really discuss that? So that puts the bedside nurse really in a bind for education opportunities, and legal consents for treatment. So we did end up proceeding with treatment. It was a difficult process for a lot of the bedside nurses. They had a really hard time with that one. And unfortunately, she did pass.

Amy Goodrich:

That definitely qualifies as a doozy. But I think those are particularly challenging, where the cultural expectation of the information the patient receives is different than ours. Those are definitely some of the most challenging cultural issues that we have, that you want to be respectful, but we're so used to informing the patient of everything.

Audience:

Yeah, from a Western culture perspective, you advocate for the patient, you have them advocate for themselves. And so that you have to really – you kind of need to be mindful of it, but you kind of have to throw it out the window a little bit when you're respecting what culture they're coming from, because they really can put up a wall with how you proceed with taking care of the patient.

Amy Goodrich:

Right. Thank you for sharing that, thank you.

Audience:

Another situation we have with clinical trials are special circumstance patients. The patients that you have to make sure are consenting and that are not feeling coerced. Whether it's because they're homeless and they feel that they have an obligation because they're getting care that they're not paying for. Whether it's an employee, perhaps of an institution that doesn't want to feel like they're not supporting the institution. Children that the parents consent, but yet we also want to get the child's feedback as well. And also in my particular area, I work at Sloan-Kettering, we have patients that maybe come in from states away, overseas. So when they're coming in, they're meeting the doctor the first time, they're often signing consent for some kind of treatment, or being told what the treatment is, they're being approached by research, they're being approached about advance directives, all those things that we have to talk about, follow those precautions. And they can get very overwhelmed. And as nurses we have an obligation to make sure nobody's kind of getting that deer caught in the headlights look and being railroaded into signing things because they don't know what they're signing any more. We have to take the opportunity to tell them to take a step back, really reflect and think, and not let people push them into signing anything right away.

Amy Goodrich:

Yes, thank you.

Audience:

Hello. I just wanted to point out at our institution, not specific with lymphoma, but with AML patients, we've had quite a few of illegal immigrants and that plays a big factor in treatment decision because you cannot be transplanted in the United States if you are not a legal citizen. So basing the type of chemo treatment you're going to be choosing

for this patient, it might be more aggressive because that's all you can do.

Amy Goodrich:
Yes. Yes, thank you.

Audience:
Hi. From the hospital where I work from, we treat a lot of lymphoma, but right now I speak from my own experience. I think I'd just like to add that the education of the patient also plays a big factor. Because my mom's a lymphoma patient and she's been a nurse for 25 years, we kind of had a hard time going through the diagnosing process, because she would want to consult every doctor in the country. But we found her the best doctor. She's now in her second cycle of chemo. But I think that plays a very big role. Their education. And sometimes knowing a lot also – and knowing not much – plays a big role in treatment.

Amy Goodrich:
I agree. Thank you. Let's just take one more. And I really appreciate all the comments here.

Audience:
Hi. I work in the Information Resource Center at The Leukemia & Lymphoma Society, so I couldn't not take this opportunity to make sure everybody knows that we have a booklet on Understanding Clinical Trials. And we can also help people do trial searches. So especially that booklet is very general and people who are having a hard time with the concept, it might be a good framework to help start the discussion.

Amy Goodrich:
Thank you. Thanks for wrapping that up with the information that LLS has.

Slide 20: Diffuse Large B-Cell Lymphoma
So I'm going to start talking now about diffuse large B-cell lymphoma because that's what my case study patient has, or that was his diagnosis.

So it's the most commonly diagnosed non-Hodgkin's lymphoma. About 31%. And so basically it's just cells gone wild. Multiple factors come into play. As I said, most patients don't have one particular thing. It's a series of hits.

There are some prognostic features. So BCL-2, which will be present in about 20 to 30% of cases, which is involved with the translocation of chromosomes 14 and 18, is associated with a more poor prognosis. BCL-6, which is another genetic marker, is associated with a better prognosis. And so we do have some way to gauge who we think is going to do better than other patients – patients that we think are going to do better than other patients. There's also this – if it's centroblastic in origin versus immunoblastic in origin. Centroblastic is germinal center B-cell and immunoblastic is activated B-cells.

Slide 21: Common Phenotypic Variants of DLBCL With Different Prognosis

So as you can see here, the GCB patients tend to do a little bit better because they have BCL-6 instead of BCL-2. And if you look at that third bullet, the overall response rates, the three year overall survival is better. It's about 77% with those with GCB than ABC. But that aside, Ki-67, which is the mitotic index for patients with lymphoma, how quickly is the cell – how quickly are they dividing – that is an independent predictor for patients with diffuse large B-cell. So we've got all these pieces, but not yet a complete puzzle of who's going to do well and who isn't.

We are very good at saying to patients, of 1,000 people just like you, this is what's going to happen to the average one. We are still not good at looking people in the eye and saying this is what is going to happen to you.

Slide 22: Current Prognostic Approaches in Diffuse Large B-cell Lymphoma

So I don't know if you all are familiar with the International Prognostic Index for diffuse large B-cell lymphoma, but we've had this since the mid-90s. Where if you looked at the age, the performance status, LDH, extranodal sites and stage, and historically we gave each of those one point, the NCCN is now suggesting that we should be splicing out age and LDH. How old really are they? Because the IPI says over 60 or under, and that's it. And the NCCN, now you can see really chunks those out. Same thing for LDH. It was a yes-no, a normal or abnormal, and now it's how abnormal is it. So it's a little different scoring system.

Slide 23: NCCN-IPI

And as you can see, the lower points you have, the better you do, alright? And I'm going to show you in a few minutes, in the IPI, APLES, a 5 was the highest score. Now you can have over 6, depending how old you are and how abnormal your LDH is.

Slide 24: Survival: NCCN-IPI vs IPI

But the difference here is the IPI is the one on the right. And on the left is the NCCN. And it's still the same picture of curves, but you can really splice out who is likely not to do well, in a way that you couldn't with the IPI. So really trying to target those patients and treat them differently, focusing on clinical trials, aggressive therapies, things like that for these patients.

Slide 25: Indications to Treat: DLBCL

So when do you treat diffuse large cell? This is not a disease that you watch and wait in general, like we do with our low grades. So a tissue confirmation is truly critical to making sure that you have this right. Once the diagnosis is confirmed, we really try to start people within two weeks. They're going to need typically a bone marrow, they need their staging work-up, most of them are going to get adriamycin, so they need an echo or a MUGA. So you have some red tape stuff that you need to get done. So you can't – these are not like Donelle's patients, where you see and admit on the same day – you usually have some wiggle room, but it's not a big window.

And then survival is in weeks without treatment. So it's very easy to say to

patients, your prognosis is really not going to be good if you don't get treated.

Slide 26: DLBCL Treatment

So how is diffuse large B-cell treated? So for patients who have non-bulky disease, limited stage, non-bulky, they can get limited chemo with radiation or full, meaning six cycles, of CHOP/rituximab with radiation. If they have bulky disease or advanced stage disease, typically they get six cycles of CHOP with rituximab. They can get it every 14 days, every 21. Sometimes there's a place for radiation for those folks, sometimes not. And then don't forget about CNS prophylaxis for patients with high risk features that we talked about on this slide. Sinus, testicular, breast, bone marrow involvement, your patients with HIV, lots of extranodal sites. Those folks, you should be considering CNS prophylaxis.

Slide 27: Case Study

So my case study is Mr. A. And he is a 39 year old who presents with rapidly increasing adenopathy in his left neck. No other symptoms. So his biopsy shows diffuse large B cell. His LDH is normal. His other labs are totally normal. He has no symptoms. And his staging reveals III-A. So above and below the diaphragm, no bone marrow involvement, no fevers, night sweats, weight loss. So a III-A. He's got a very supportive wife and a cute little daughter. He came to the United States as a child from Mexico. So essentially is Americanized as you can be, but does come from a strong Mexican background.

Slide 28: Case Study

So his variant info. So he's got CGB, which is good prognosis. He's got BCL-6, so his estimated survival at three years is 85%. So when you talk to him you're saying, you know, this is – you're at a high incidence of being cured, we're going to treat this hard, we don't know who this 15% is going to be who aren't going to do well, but the odds are that we're going to be able to do a good job with this. So overall from his variant information, he has a favorable prognosis.

The little glitch here is that his Ki-67 is high. So what do you do with that when you're talking to a patient? You make sure they understand that, that we have some conflicting information. The Ki-67 is high, which is not good, but the variant results are good. So we're going to hit it hard and just try to get rid of this and have this be just a bad dream that you had, like Christine over there. Writing a book in 12 years. I wish everybody could do that.

Slide 29: Current Prognostic Approaches in Diffuse Large B-cell Lymphoma

So if we look at his NCCN prognostics. His age, he's 39, so he doesn't get a point. LDH is normal. His performance status is great, he's working full-time. He does have advanced stage disease. And he does not have extranodal involvement. So he on paper has very low risk disease with our International Prognostic Index Scoring.

Slide 30: NCCN-IPI: Mr. A.

So if we look at him, he's a 1. So his five year overall survival should be 96%. If

you see there in the middle. And progression-free survival 91% at five years.

Slide 31: Case Study

So what happens to him? He gets six cycles of CHOP and rituximab. Post-therapy he's got a residual mass in his mediastinum. So we got a PET and they said, well, we're going to say the PET's negative, but this thing in his mediastinum is not quite cold, so we should just watch this.

So three months later he gets another PET/CT done and the node is the same size, but it's a little brighter on PET. So what do you do with that? Not sure what to do with that. So wait another three months.

And by six months after therapy, he's got stuff exploding everywhere. And this guy should be in that number zero to 1 category, but obviously is not.

Slide 32: Case Study

So we re-biopsy him and that is so critical in lymphomas, to re-biopsy and not assume anything about what you think is going on without pathological confirmation. So he's got essentially primary refractory disease. He gets RICE for four cycles and the mediastinum went cold, but he had this new supraclavicular node that did not go cold after the RICE. So we spot-welded it with some radiation and took him to allotransplant from a sibling. He got it on-study, so he was on a trial for his transplant. And two months after transplant he's progressing again, which is very sad.

Slide 33: Case Study

He did, in the midst of all this, develop graft-versus-host disease, which is really the way the allotransplant works, right? So we did not get our bang for our buck out of that transplant. Five months after the transplant, he presents with diplopia while he was still on steroids for his GVH. Worked him up and down. And he was somebody who would call and downplay everything. But called one day, saying, you know, my eye is a little bigger, my left one's a little bigger than the right one. And he came in and I could not believe that he was saying it was a little bigger. It was grossly abnormal. So he ended up, the PET showed that he had a mass behind his orbit. With all sorts of other disease as well.

I'm sorry, let me go back here.

Slide 34: Case Study

So we radiated his eye. We gave him some rituximab. He had some initial improvement in his eye, but then progressed systemically.

He's now nine months after the transplant and for those of you who have patients who get transplants, you know that their counts are funky for a long time and they – to try to treat somebody so tight after transplant is hard. He got lenalidomide and rituximab. He did respond somewhat to it. But then his counts went to the garbage can and we had to delay. He ended up progressing.

We did a marrow just to make sure his bone marrow wasn't packed because he had such profound cytopenias. His bone marrow was negative. It was just completely

beaten up from all the therapy.

Slide 35: Case Study

We tried to pulse him with steroids. He developed neuro-symptoms again. He now has brain lesions. He gets radiation. He's almost a year after transplant. He starts progressing everywhere. Continued cytopenias. It's almost impossible to treat people like this. And he ends up dying 11 months after his transplant.

So what were the – so this is like a bad on bad story – but how did the cultural aspects play into this?

Slide 36: Mexican Cultural Implications

So if you look at the literature for folks who are Mexican in background, there's a strong reliance on family. So I'm in Baltimore and so he lived near Baltimore. His family was all in Texas. So strong reliance on family. The father or the oldest male holds the greatest power. They may tend to be the ones who have the biggest say in health decisions for other people.

I thought this was interesting, this machismo definition, which I had never looked up before. It's sense of honor for Hispanic males. Women are expected to be the primary force of holding the family together, including caregiving.

Slide 37: Mexican Cultural Implications

So tend to have lots of family involvement, lots of faith involvement, lay healing, family does a lot of the death and dying care, and a very low rate of hospice utilization. Which I didn't know any of this when I'm taking care of this guy, so thank you, Lauren.

Slide 38: Discussion Question

So what strategies have you used or seen in others?

Let's save this for hospice, right? Because I'm sort of running out of time here. Let's save this one for the end. Is that good, Lauren? Okay.

Slide 39: Mr. A.

So what happens to this guy? He's got a non-Hispanic wife. Okay, so all those caregiving and female expectations, she's not – not that she didn't take wonderful care of him, but she was not culturally sensitive to all that. He was the oldest male in the family. His father had died. He was a very significant distance from his family. He did not discuss his prognosis, so I kept saying to him, if you want to see your mother again, she needs to come here, you need to get your mother here. Never did it. Died at home without hospice.

So sort of just a very sad situation. Some of it was cultural, for sure, that he did not want to reach out to the females in the family, to let them know how bad things were. And his wife definitely didn't. She wasn't cued into the fact that she needed to be doing all that. She was trying to be respectful to his wishes. So it was just a bad situation.

But I do want to come back to that at the very end when we have time, because Donelle has great questions for you, too, in the middle of hers. I don't want to leave her with no time.

Slide 40: Key Take Aways

So hopefully you learned here there's a lot new in lymphoma. Ibrutinib, obinutuzumab. There's a lot coming. So Lauren told you that they're funding – LLS funds a lot of research.

So diffuse large cell, which we talked, in our case study, we've got good prognostic tools and tests, but they're not perfect. This guy really shows us they're not perfect. And so it's critical for you guys to have some understanding of who's likely to do well and who's not. But keeping up is the biggest challenge because most of you see every disease under the sun. So hopefully having good resources and places to go to look for these things is something that you have access to. And the outcome for the patient is not always about prognostics. So even though we're making a lot of progress, there's still more that we don't understand than we do, certainly for lymphomas. And patient factors will always impact outcomes.

Slide 41: Question and Answer

And so I think that is my last slide. And I'm going to turn this over to Donelle. And then we can do questions and answers at the end.

Slide 42: Acute Myeloid Leukemia

Donelle Rizzuto:

Good afternoon. Thank you so much for coming. My name's Donelle and I am really honored to be talking on behalf of The Leukemia & Lymphoma Society. They just are such a great organization.

And what I want to talk with you about today is acute myeloid leukemia and understanding the basics, treatment options, and how nursing can really hopefully help affect better patient outcomes.

Slide 43: Acute Myeloid Leukemia

So what is AML? It's an aggressive form of blood cancer in which too many abnormal – I'm sorry – too many normal myeloid blood stem cells become abnormal leukemia cells.

Slide 44: AML Incidence 2014

So AML is actually relatively rare. There's going to be a little bit less than 20,000 cases diagnosed in 2014. The majority of this, of course, is going to be in adults. And there's going to be about 10,500 or so deaths in 2014 from AML. Again, the majority will be in adults.

Slide 45: Risk Factors

So talking about risk factors. Probably the main for risk factors is people who have had previous chemotherapies, alkylated agents, platinum drugs or anthracyclines, radiation, and I'm sure most of you know certain blood cancers, MDS can transform into AML and that definitely is a big risk factor, and of course, age is also. And it's on my

second slide. Also benzine exposure, which is cigarette smoke. People who've had myeloproliferative neoplasms, such as P. vera, central thrombocytosis, myelofibrosis are at risk. The genetic syndromes, Down Syndrome, Fanconi's.

So AML is a disease of aging, so usually people over 60 years old are at biggest risk for getting AML.

Slide 46: Risk Factors

And I'm sure many of you have probably had patients or patients' family members ask, you know, my dad or one of my family members just got diagnosed with AML, what's the risk for me and my family?

So there is a small risk if a close family member's diagnosed with AML. Like a parent or sibling. However, even if that happens, the risk to family member is still very low.

So one of the main things that's really important in how we treat AML and why clinical trials are so important in this disease, is really knowing the molecular and cytogenetics of AML when a patient's diagnosed.

Slide 47: The Role of Molecular and Cytogenetic Testing in Prognosis and Treatment

So some of you may wonder why is I see patients and we just treat them with chemotherapy and there's no intent for them to go for a bone marrow transplant unless they relapse? And then you have other patients that walk through your door, we start chemotherapy immediately, and we also start the ball rolling to get them to transplant immediately.

And the difference between these two patient populations is determined by – sorry, determining treatment and prognosis is based on cytogenetic and molecular studies.

Slide 48: Cytogenetics

So cytogenetics is a patient's karyotype. We're looking at chromosomes. And karyotyping in AML is actually looking at the chromosomes of the leukemia cell. People with AML can have normal and abnormal cytogenetics. And older people, people with previous chemotherapies, and a history of blood cancers, those are patients that are probably going to have abnormal cytogenetics.

Slide 49: Molecular Studies

Some of you may have heard of molecular studies. There's just about three that we really look at, but the main ones that you may hear are FLT3 positive AML or NPM1 positive.

And so FLT3, unfortunately, is a very bad finding with leukemia, with AML. It's unfavorable. People typically – it's very hard to get them in remission, and when we do get them in remission, it's very short, and they relapse frequently.

NPM1 positive AML is actually favorable, as long as they are not also FLT3 positive. So the NPM1 is actually a good abnormality to have.

So once we have this information, why is it so important? And one thing that I

want to talk about, too, is that we get these patients, they get a diagnosis of AML, it's really important – we have time as long as the patients are stable, that we can get make sure we have all the tests we need as far as the cytogenetics and the molecular studies – it's really important to try to get this information, so we do give patients the options or make sure we give them the correct treatment that's going to be more beneficial. Instead of just getting them in the hospital and getting them standard therapy, we want to make sure that the treatment that we're going to give them is actually going to hopefully do some good with their leukemia.

Slide 50: Prognosis

So once we're able to find out cytogenetics and molecular studies, we're able to place patients in one of three risk groups. Favorable, intermediate and poor.

And so this risk refers to what happens with standard therapy. And it may not apply to clinical trials or newer therapies that we're treating AML with.

Slide 51: "Favorable" AML

So favorable AML. We wish everybody would have favorable AML. It would be really nice.

So inversion 16. And you'll see the INV 16, is how you'll see it listed on the cytogenetics report. Translocation of the 8 and 21st chromosome. And somebody who has normal cytogenetics that is NPM1 positive, but FLT3 negative, is also in this favorable AML.

So 80 to 90% of patients are going to achieve a complete remission with just standard therapy. So very good statistics. And then 70% will achieve a cure with standard therapy and without receiving a stem cell transplant. A patient could opt to go on a trial in this type of AML, but usually most people when they see the statistics, they're pretty confident and feel like these numbers are pretty good, so the majority of people with this type of AML are usually just going to receive standard therapy.

Slide 52: "Intermediate" AML

Intermediate AML is patients who have normal cytogenetics. There is no NPM1 or – I'm sorry, the NPM1 and the FLT3 are both negative. So it's pretty dramatic how much this changes, because the overall survival rate at two years with intermediate AML is 30% with standard therapy, and 30 to 40% with standard therapy and a stem cell transplant. So that's a pretty dramatic decrease in success rate, just from good risk AML to intermediate.

So patients in this group could choose standard therapy or they could also choose a trial. And for some of my patients, they're not sure what's the right thing to do, and so if people start on a clinical trial or start with standard therapy, if one of those is not successful, then we could always still progress to a trial or progress back to standard therapy. So we do have options there.

Slide 53: "Poor" AML

And the last group is poor risk AML. And so this is somebody that has very bad

cytogenetics and you can see this is actually a 29 year old's cytogenetics. And when you look at this, you see a lot of information. And what really is important, probably one of the key factors when you look at this, is deletion 5 or deletion 7 in this abnormal cytogenetics. And if people have more than three to five abnormalities, we call it a complex cytogenetics. It's just more difficult to treat obviously.

Slide 54: "Poor" AML

So I made a mistake. The trisomy 8, that is incorrect. That is somebody who actually has an extra copy of the eighth chromosome, and that actually is more of an intermediate abnormality. So my apologies for that. But the monosomy 5 and monosomy 7, that's when there's a deletion of the arm of the fifth or seventh chromosome, and that is definitely an indicator of poor risk AML.

So the rates even are very grim. Less than 5% success rate of complete remission with standard therapy and poor risk AML. And a 10 to 20% with standard therapy plus a transplant. So obviously people are going to get that information and think that probably I have a better chance with a clinical trial to achieve a remission.

Slide 55: Clinical Trials: Talking With Patients

So clinical trials. And I think key factors in talking with patients, I definitely want to acknowledge that I think there's a big hole in our healthcare system where a lot of patients are only able to get clinical trials at big academic centers or at the larger hospitals. So we have patients in smaller communities that we don't really have a lot of clinical trials available. We have patients that come to us and have to move to Seattle and for rent it's $2,000 to $3,000 a month. So not only getting diagnosed with a life-threatening illness, then they have to uproot their life, have a huge out-of-pocket expense to go and get treatment. So hopefully in the future that we will be able to really try to push to get more clinical trials available in the community settings, because it really puts these patients – I think it's a lot for any patient to have to go through with that.

Slide 56: Nursing in Educating Patients

So how can nurses help talk to patients about clinical trials? And it sounds like from the last talk, that there's a lot of people that already deal with clinical trials on a regular basis. So what we like to talk with our patients about is that clinical trials, why they're there is to give patients options to potentially achieve better results than standard therapy, in potentially all risk groups, but mainly in intermediate and poor risk AML.

Many clinical trials that we have available at our facility right now, they're drugs that are already approved for AML, we're just using them differently. One trial we do, we do decitabine priming as an outpatient for five to ten days and then we admit the patient after to receive meds. So what they are doing is trying to prime the leukemia cells, so when we give them the bigger chemo, that they will be sensitive and hopefully die off.

And we definitely have clinical trials that are really focused on the older patient, with the emphasis that they're less toxic, and with the hope that we'll be able to keep them out of the hospital during this treatment.

Although everybody reacts differently, a majority of our patients are able to stay out of the hospital on these less toxic treatments, and very happy that they don't have to

be admitted to the hospital.

Slide 57: Diversity in Educating Patients

So some of the diversity in educating patients. I have a pretty diverse – just as far as age – the majority of my patients are over 60, but I have 19, 20 year olds, 30 year olds, so I've got kind of this huge range of patients. So with me, my diversity with patient education is just the age range that I deal with.

So obviously my case study is going to be focusing on the older adult. And I want to get some of your – have you guys talk here in a minute about what some barriers you've ran into with patients. I mainly get some push-back from older patients about clinical trials. And common reactions are that I don't want to be treated like a guinea pig, the drug company doesn't care about me, they just want me to go on this trial so they can make money.

Slide 58: Ethical Issues for Nurses

So ethical issues in nursing. I think all of us deal with this every day. I've got a couple of patients I want to talk about.

Slide 59: Case Study - Margo

The first is just Margot. And this is really just how different two older patients did on a clinical trial.

So Margot is 70 years old. She was normal cytogenetics. She was NPM1 positive and FLT3 positive, so she automatically went into a poor risk AML. So she in June of last year started a trial and this was a 35 day cycle, where she was on an oral drug called tosedostat and she got randomized to cytarabine days 1 through 5 each – every 35 days.

She got into a remission after the first cycle. She did have some side effects. She definitely had a rash, which was a common side effect with this tosedostat. It was manageable. She struggled with nausea. And she only was hospitalized two days out of the entire treatment before she went to transplant.

She ended up going to transplant in November. She's completed the transplant. She's doing very well.

So this is I think ten years ago, thinking that a 70 year old would be going to transplant, I think we're looking at getting these older patients to transplant more frequently. We actually just had a 79 year old that we sent to transplant in the last couple of months, so we'll see how that's going to go.

Slide 60: Case Study - Wima

The next one is Wilma. And Wilma's 79 years old. She was normal cytogenetics. She was NPM1 and FLT3 negative. But she also had a history of MDS. So she also went a little bit more into the poor risk category.

So she also went on the oral study, the oral tosedostat, and she also got randomized to the cytarabine, days 1 through 5.

She got into a complete remission as well after the first cycle.

She had a very, very severe rash. She started having some reaction at her PICC site, that we thought was maybe from the dressing. And it basically just proceeded to spread to her entire body, along with arm swelling, leg swelling. It was pretty dramatic.

Since she did get into remission after the first cycle, she decided she would see if she could tolerate one more cycle. We took her off some of the prophylactic medications to see if that was contributing to the rash. But again, it was very dramatic and she just declined to do any further treatment after that.

So she came back to us I believe in August and she had relapsed. We did one dose of kind of a targeted therapy for her and she ended back up in the hospital and just came back to us and said I don't want to do any more chemo, I'm done, I just want to do supportive care.

She was feeling really poor at this point. She had bone pain, she couldn't eat, she had no energy, weakness. And so we decided to put her on prednisone, 60 milligrams a day, and we just had her stay on that until she was feeling better. She got a good response from it. And then we just had her decrease 5 milligrams about every five days until she got to a dose that she was feeling good on.

Slide 61: Case Study - Wima

Initially we had her come in about every 7 to 10 days for occasionally she'd need some red cells. We scheduled her for hydration. But after about two weeks she really didn't need anything. She started coming almost every two to three weeks and she was back to her normal baseline, she was doing fantastic, with her blood counts, her peripheral blasts, and CBC, everything was really stable.

So her daughter comes in and says, well, Mom's doing so well now, why don't we consider doing another trial? So we did a low dose subcu Ara-C and a low dose decitabine as an outpatient. She did pretty well. We definitely had some issues. But the thing with Wilma is she traveled two hours each way from Bellingham to come to Seattle Cancer Care. So we tried to limit how many times she was coming in a day.

Slide 62: Case Study - Wilma

Right before Christmas her daughter came to us, kind of broke down and said, you know, my mom's been having these intermittent fevers for two weeks, she's taking 3,000 to 4,000 milligrams a day of Tylenol because she knows if she tells you she has a fever, you're going to put her in the hospital and that's not what she wants. So the daughter was overwhelmed, she'd been helping care for her mom. Also Wilma's husband was at home with dementia and Wilma was the primary caregiver for him, so it ended up being a very complex social situation.

So we discussed nursing placement, palliative care. We had already discussed all these options. Unfortunately, the patient and family did want to do palliative care, but their understanding of palliative care was 24 hour nursing care in-home, not paid for by them. So we had to kind of make that a reality.

So with the daughter being so overwhelmed and the patient definitely having fevers, we admitted Christmas Eve, hoping it would just be a short stay for her. She, of course, developed a lot of issues, kidney failure, she got hospital-induced dementia, respiratory failure, and the family decided on comfort care, and she died in January.

So I think with how many antibiotics and antifungals and how many studies we have available right now, patients can just continue to keep going and we're keeping them alive a lot longer. But when somebody comes in and says they don't want other treatment and then the family member – they decide to do treatment mainly for a family member – you know, how do we really address this? And this is an issue we're trying to work with with our team, of really making the patient's wishes known.

Slide 63: Ethical Issues With AML

So I think a big ethical issue is what we just talked about, you know, patients that want to stop or start treatment, but the family wants them to do the opposite.

And for I think a lot of people, they're wanting to make their family members happy, so there's a lot of pressure on a patient at critical decision-making points.

Of course, there's cultural differences to gender, age, religious beliefs or spirituality.

I think a lot of people, these patients, we keep them outpatient. They have some issues, but they do overall pretty well. And so have them understanding what the outcome will be at times.

And it's just definitely difficult to communicate bad news to patients and their family and have them be able to cope with that effectively.

So we wanted to talk about ethical issues, but I think should we just kind of open this up to just general questions that you might have, whether it be with ethical issues or any other general questions you have for us?

Slide 64: The Leukemia & Lymphoma Society Resources

And again, at the end of this, there's also some great information from The Leukemia & Lymphoma – on their website and what's available on the different disorders.

Slide 65: The Leukemia & Lymphoma Society Resources

Lauren Berger:

Are there any questions? If not, thank you for joining us. And we hope that you will stay in touch with us at The Leukemia & Lymphoma Society. Our Information Resource Center information is in the workbook. They're available from 9 AM to 9 PM Eastern Time, for your questions, for your patients' questions, clinical trials, treatment issues, financial support, copay assistance, and we're happy to help.

Slide 67: Thank You!

So thank you so much to Amy and Donelle for sharing your information as well as sharing your case stories.

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