

Hodgkin Lymphoma Update: Making Treatment Decisions

Mary K. Gospodarowicz, MD, FRCPC, FRCR (Hon.)
May 29, 2007 • 12:00pm ET

OPERATOR: Hello, everyone, and welcome to *Hodgkin Lymphoma Update: Making Treatment Decisions*, a free telephone education program. It is my pleasure to introduce your moderator, Peyton Mason.

PEYTON MASON: Thank you, and hello everyone. My name is Peyton Mason. I am the National Director of Patient Services Programs for The Leukemia & Lymphoma Society. On behalf of The Leukemia & Lymphoma Society, we thank you for choosing to spend this hour with us today and we welcome all of you.

Today's program, *Hodgkin Lymphoma Update: Making Treatment Decisions*, is sponsored in full by The Leukemia & Lymphoma Society, and features Dr. Mary Gospodarowicz. We welcome Dr. Gospodarowicz and thank her for sharing her time and expertise with us today.

You all should have received a packet of information that includes brochures about some of the Society's services, flyers to order our free booklets and Dr. Gospodarowicz's biography. We encourage you to look through the materials at your leisure.

You will also find in your packet an order form for The Leukemia & Lymphoma Society's materials and an evaluation form for you to fill out for today's program. For nurses and social workers, you can receive continuing education credit for today's program, and we've included an evaluation form marked specifically for you in the packet. Please return that form in the envelope provided to claim your one hour of credit. All other program participants may use that envelope to return your program evaluation.

After our keynote presentation, we will open the program to take questions from our telephone audience. We have close to 1,000 individuals participating today via telephone from all over the country, in addition to several international participants from Canada, Greece, Russia, Barbados, England and Taiwan. And healthcare professionals from Pakistan, Mongolia, Iraq, India and Uruguay. We welcome everyone on the line.

If we are not able to get to your question today, you can call the Society's Information Resource Center toll-free. That number is 800-955-4572. That number is on the materials in your packet. Dialing that number will connect you with an information specialist, a Master's level social worker or health educator, and our information specialists can answer your questions or help you obtain more information. That number again is 800-955-4572. The IRC's hours are between 9 AM and 6 PM Eastern Standard Time, Monday through Friday.

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PEYTON MASON: We are also audiotaping and transcribing today's live program for future posting on the Society's Web site. The program archive will be available to you to access in a few weeks on www.lls.org/lymphomaeducation.

The Leukemia & Lymphoma Society provides critical information and support to all patients, families and caregivers touched by blood cancer. The Society has 68 chapters in total, including three chapters in Canada, and offers a comprehensive array of free services to patients and families. The Society's mission is to cure these blood cancers and provide support for patients and their families. We hope that today's program is a step forward for you in providing up-to-date information on Hodgkin lymphoma.

It is now my pleasure to introduce our guest speaker, Dr. Gospodarowicz. Dr. Gospodarowicz is Medical Director of the Cancer Program at Princess Margaret Hospital and University Health Network and Regional Vice President of Cancer Care Ontario. She is also Professor and Chair of the Department of Radiation Oncology at the University of Toronto and Chief of the Radiation Medicine Program at Princess Margaret Hospital. Dr. Gospodarowicz is engaged in the active clinical practice of radiation oncology, treating patients with malignant lymphomas. Her research interests include clinical trials, evaluating the role of radiation therapy in lymphoma, prostate cancer, bladder cancer and testicular cancer. She has authored more than 250 peer-reviewed papers, books, chapters, and letters. Her complete biography can be found in your packet.

And it is now my pleasure to turn the program over to you, Dr. Gospodarowicz.

DR. GOSPODAROWICZ: Thank you very much, Peyton. Thank you, everyone, for joining the conference call. It is my pleasure to talk to you briefly today about Hodgkin lymphoma.

Hodgkin lymphoma is one of the most curable malignant diseases that are present today. It is not a common cancer. This year it is projected that in the United States there will be just over 8,100 new cases of Hodgkin lymphoma diagnosed. It is expected that just over 1,000 patients will die of Hodgkin's disease.

Currently over 80% to 85% of all patients diagnosed with Hodgkin's disease can expect to be cured of Hodgkin's disease. This is one of the triumphs of modern treatment of cancer.

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DR. GOSPODAROWICZ: Patients who are affected by Hodgkin's disease are usually younger patients. The median, the most common age of presentation, is in the late 20s to 30s, although Hodgkin's disease can occur in children and can also affect the elderly, although it is much less common in patients over 50 years of age.

The presentation classically is with patients finding a painless lump, usually in the neck, sometimes in the armpit, sometimes in the groin. But a vast majority of patients who present with Hodgkin's disease will have disease in the upper part of the body.

Occasionally patients can present with other symptoms. They can present with persistent cough and shortness of breath if their Hodgkin lymphoma is located in the chest. They can also present with symptoms such as intractable itching, pruritus, itching of the skin, that does not respond to medication.

Occasionally patients with more advanced Hodgkin lymphoma can present with fever and unexplained weight loss. Usually quite a significant weight loss. Occasionally patients can also have night sweats. It's very characteristic, sweating at night associated with Hodgkin's disease, where patients develop drenching sweats of the whole body and not just the usual neck area or chest area. These so-called systemic symptoms of Hodgkin's disease are thought to be due to Hodgkin's cells [Reed-Sternberg cells] producing various cytokines that cause these symptoms.

The diagnosis is usually achieved by biopsy and, unlike in other types of lymphomas, needle biopsy is usually not sufficient. It's usually required to excise a lymph node or part of the lymph node to have adequate amount of tissue for the pathologist to do special stains and to make sure that there is a firm diagnosis of Hodgkin lymphoma.

Hodgkin lymphoma can be confused with different types of non-Hodgkin lymphoma. And since the treatment is different, the high quality of correct precise pathologic diagnosis is really the first step before treatment is considered.

Once we know that the patient has Hodgkin's disease, it's also important to know what type of Hodgkin's disease. There are two main categories of Hodgkin's disease. One is called classical Hodgkin lymphoma and the most common subtype in the classical range is nodular sclerosing Hodgkin lymphoma, Nodular sclerosing Hodgkin lymphoma occurs in approximately 70% of all patients with Hodgkin's.

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DR. GOSPODAROWICZ: It is characterized by the fact that when one looks under the microscope, amongst the Hodgkin's cells there are strains of fibrosis or fibrous tissue, which is the tissue that forms the scars. The importance of this knowledge is that sometimes after treatment of Hodgkin's disease, there could be persistent abnormalities on X-rays or persistent small lumps, which may be benign because they just are residual fibrosis or scar tissue after malignant cells have been eliminated. So nodular sclerosis is a very common form of Hodgkin's disease.

The second type of classical Hodgkin's disease is mixed cellularity Hodgkin lymphoma. This is a somewhat more aggressive of histological form, although just as curable.

The other two are lymphocyte depleted Hodgkin lymphoma, a very uncommon type right now, and lymphocyte-rich classical Hodgkin lymphoma, which is different in outcome from the other forms.

Besides the classical Hodgkin lymphoma, the nodular lymphocyte predominant Hodgkin lymphoma, and that's a mouthful, nodular lymphocyte predominant Hodgkin lymphoma, is a unique pathologic entity. It's a unique disease. It usually presents with very limited disease, and treatment is somewhat different. Therefore I want to emphasize that knowing the pathologic subtype is actually important for treatment decisions.

Once the diagnosis has been established, the physician looking after the patient needs to determine the extent of the disease. Because the biopsy establishes what type of Hodgkin lymphoma the patient has. Staging, or what we call staging investigations, determine how extensively it has spread and where it is present in the body. So, for example, currently the routine staging investigations are based on imaging, that's diagnostic radiology. In most centers the patient undergoes CAT scans, that's computerized tomography imaging. CAT scan of the neck, chest, abdomen and pelvis. We basically put the patient in a computer, and we can image all the areas where lymph nodes are present to see whether there are other areas of involvement. CAT scan also will show us whether there is involvement of the lungs, liver, other organs, and basically will be very helpful in establishing disease extent.

In addition, patients have blood tests. Patients who present with more advanced Hodgkin's disease should have a bone marrow biopsy to make sure that there is no spread of Hodgkin's to the bone marrow. Fortunately spread to the bone marrow is very uncommon.

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DR. GOSPODAROWICZ: Therefore, bone marrow biopsy is not required in patients who present with Stage 1 and 2 disease and who are asymptomatic and therefore don't have fever, night sweats, weight loss and don't have bulky disease.

Once the staging is completed, the physician has the knowledge not only of what type of Hodgkin's disease the patient has but also of how extensive it is and where the disease is located, which are important for evaluation of the treatment effectiveness.

In Hodgkin's disease, and in all cancers, we have staging systems. Cancer staging is really a classification that lets us communicate what the anatomic extent of cancer is. Is it localized in one area of the body, other areas of the body, where it is.

The staging system for Hodgkin's disease has been developed now almost 40 years ago and hasn't changed much in that time. Very stable. It's called the Modified Ann Arbor Staging System, for the place where the agreement on the staging system was arrived at. It divides Hodgkin's disease into four stages. Stage 1 is assigned when patients have single lymph nodes or single lymph node region involved. So, for example, one side of the neck, when disease is limited to, let's say, right neck or right axilla, which is the armpit. Stage 2 is when there are lymph nodes present in more than one lymph node region, more than one area. But it is limited to one part of the body, either the upper half of the body above the diaphragm, so the chest, neck and underarms, or below the diaphragm, the abdomen and pelvis. So, in Stage 2, patients can have a number of lymph nodes and a number of lymph node areas involved, but it's limited to one part of the body. Stage 3 Hodgkin's disease is when there's involvement of both sides of the diaphragm. It could be a patient who has a lymph node in the neck and a lymph node in the abdomen. The total amount of disease in Stage 3 may be quite limited, but extends to various parts of the body. Stage 4 Hodgkin lymphoma is disease where in addition to involvement of lymph nodes, there is involvement of one or more extra-lymphatic organs such as the lung, liver, bone marrow or bone, or other parts of the body. Stage 4 Hodgkin lymphoma is much less common than Stage 1 and 2. In fact, Stage 1 and 2 Hodgkin lymphoma is probably present in about half of the patients who develop Hodgkin lymphoma.

Hodgkin lymphoma can progress in an orderly manner. So, occasionally patients who develop Hodgkin lymphoma, if they go untreated or undiagnosed, can progress from Stage 1 and 2 to Stage 3. However, occasionally the Hodgkin lymphoma will present de novo or right at the beginning with Stage 3 disease.

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DR. GOSPODAROWICZ: We think that's probably related in part to the biology of the disease. If the patient presents with Stage 3 or 4 Hodgkin lymphoma it's not necessarily always because there was a delay in diagnosis. It may be an inherent part of the disease characteristic.

In addition to the staging classification of Stage 1, 2, 3, 4, we assign descriptor Stage 1A or Stage 1B. Descriptor A means that the patient had no systemic symptoms at presentation. Systemic symptoms are unexplained fever, drenching night sweats or weight loss of more than 10% of body weight. Descriptor B means that symptoms were present. Again, although these symptoms are more common in patients with advanced Hodgkin lymphoma, they can happen in Stage 1 disease, so they are an independent factor.

The other prognostic factors that we look at in patients with early stage Hodgkin lymphoma is whether the patient presents with bulk disease, a de novo mass that's more than 10 centimeters in diameter, that's 4 inches in diameter, is considered bulky. Where it is really important is particularly in the chest, in the thorax, where between the two lungs there is an area called the mediastinum. It's a very common location for involvement of Hodgkin's disease. When patients present with a mediastinal mass that's more than 10 centimeters on CAT scan or occupies more than one third of the width of the thorax, it is considered unfavorable disease. It requires more treatment.

Now the terms of favorable presentation and unfavorable presentation, today in the treatment don't always mean that the outcome will be worse following treatment, but they are a signal to the treating physician that the treatment needs to be more intensive. It is commonly thought that patients with Stage 2 or 3 cancer will do worse than patients with Stage 1 cancer. To a certain extent that is true. But when the treatment is very effective it may merely mean that the advanced stage just requires more treatment, but the patient also can be cured.

Patients who present with Stage 3 and 4 Hodgkin lymphoma, who have disseminated disease in various parts of the body, also have a different set of prognostic factors. Once the disease is advanced there is great variety in presentation. Patients who are older, have Stage 4 disease, have very high white cell counts, have a low albumin level – that's a protein level in the blood – have low hemoglobin or have very low lymphocyte count or indeed, men rather than women, have a worse prognosis in advanced Hodgkin's disease. When we look at outcomes of patients who present differently, we can actually refine the prognosis according to these parameters.

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DR. GOSPODAROWICZ: A number of years ago there was a big study that defined these parameters, that formed the International Prognostic Index in advanced Hodgkin's disease. These factors may be used to recommend more aggressive treatment or they can be used in patients who are in clinical trials to make sure that we compare patients with different prognoses.

These days, Stage 1 and 2 Hodgkin's disease is usually cured. The cure rate exceeds 95%. The classical treatment of Stage 1 and 2 Hodgkin's disease was with radiation therapy. In the last two decades it has been with combined modality therapy, reducing the amount of radiation and giving more chemotherapy, which resulted in less toxicity and improved outcome.

There are clinical trials right now that indicate that the vast majority of patients with Stage 1 and 2 Hodgkin's disease could possibly be treated with chemotherapy alone with about an 85% cure rate with first treatment. The controversy right now exists of whether it's better to treat Hodgkin's disease with short course of chemotherapy – and we usually use ABVD chemotherapy of doxorubicin, bleomycin, vinblastine and dacarbazine. The current practice guidelines for treatment of early-stage, low-risk Hodgkin's disease suggest that patients can have as few as two courses of ABVD chemotherapy, followed by involved field radiation with a reduced dose of radiation, to 30 Gray, with an over 97% likelihood of never having a recurrence of Hodgkin's disease.

Patients who have an unfavorable presentation, Stage 1 and 2, require more chemotherapy and combined modality therapy, at least four or sometimes six cycles of ABVD, also followed by involved field radiation.

Patients with advanced Hodgkin's disease, Stage 3 and 4, can be treated with six to eight courses of ABVD or a regimen called BEACOPP, which includes bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine and prednisone. This multi-drug regimen used in advanced Hodgkin's disease results in an exceedingly good cure rate, but carries a small risk of leukemia. Therefore, in North America, it is rarely used and only for patients with very aggressive presentations of advanced Hodgkin lymphoma.

Patients who recur after treatment can recur in two ways. There is a very small number of patients, a few percent, who are refractory to treatment. The ABVD chemotherapy causes disease regression in the vast majority of patients. Less than 10% will respond only briefly or not respond to ABVD and progress. This is a very grave situation that requires aggressive treatment and high-dose chemotherapy with stem cell support.

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DR. GOSPODAROWICZ: High-dose chemotherapy/stem cell support can also cure recurrent Hodgkin's disease, that is, when the disease went into remission, a patient was well for a year or two and then developed disease recurrence. Currently it is not recommended that the high-dose chemotherapy and stem cell rescue be used up front in treatment, mostly because the results of treatment with primary ABVD or BEACOPP are so good, and because high-dose chemotherapy and stem cell support actually are much more toxic.

The treatment of Hodgkin's disease has been changing over the last few years and as I said, Stage 1 and 2 disease is highly curable. However, when we follow patients with Stage 1 and 2 Hodgkin's disease who have been cured, their survival of 20, 30 or 40 years is not 100%. It's not even 95%. It's somewhere around 80% to 85% because the treatment that was given 15 to 20 years ago was based on the aggressive use of radiation therapy for Stage 1 and 2 Hodgkin's disease. Radiation therapy is the single most effective weapon against Hodgkin's disease, but it carries late side effects.

In 1970s and 1980s the chemotherapy that was available for management of Hodgkin's disease was that of MOPP chemotherapy that included mechlorethamine, vincristine, procarbazine and prednisone. And M, which stood for nitrogen mustard, is an alkylating agent that has been associated with inducing leukemia. So although patients were cured of Hodgkin's disease, this treatment carried with it a small but definite risk of acute leukemia that was fatal. And because of that, the treatment was billed so that only patients who had to have chemotherapy had chemotherapy and other patients were managed with radiation. This was very safe treatment, but unfortunately a small but significant proportion of patients who have extensive radiation treatment will be at risk for second cancer. The second cancers can occur anywhere from five to ten to twenty or thirty years after radiation therapy. The second cancers have been shown to be related both to the extent of radiation treatment and the dose of radiation treatment. Therefore, the current management of early stage Hodgkin's disease calls for reduction in radiation fields. We no longer treat extended fields prophylactically to reduce risk of recurrence. We only treat very precisely the areas that have been involved with Hodgkin's disease and the doses of radiation therapy have gone down from 44 Gray that was standard before to 25 to 30 Gray, almost a 30% to 40% reduction in radiation dose.

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DR. GOSPODAROWICZ: We also know much more about who is at risk for second cancers. For example, we know that children or young women, women under the age of 30, who have radiation to the breast are at high risk for developing breast cancer 15 to 20 years following radiation for Hodgkin's disease.

We can introduce screening very early in these women and although there are some women that will develop breast cancer following treatment for Hodgkin's disease, the breast cancer, when it's picked up early, can be cured.

Patients who have chest radiation also are at risk of lung cancer. It's very important to counsel the patient and educate to absolutely stop smoking and prevent exposure to tobacco. We have very robust data right now that suggest that patients who received chest irradiation for Hodgkin's disease 10 to 20 years ago, if they have not smoked their risk of lung cancer is about 4 times that of general population – all people. If they continue to smoke after the treatment of Hodgkin's disease after chest irradiation, they may have as high as a 25 to 40 times increased risk of lung cancer, depending on whether they had radiotherapy alone or whether they also had chemotherapy.

So the current trend to minimize treatment in Hodgkin's disease is aimed not at improving the cure rate – we are already there, curing most patients with favorable Hodgkin's disease – but at lowering the risk of late complications.

The other trend is to use chemotherapy alone. There are other newer combinations of chemotherapy being tried in clinical trials. However, when you deal with a cure rate of about 95% and higher, it is important not to change the treatment outside of clinical trials because if we lower the cure rate from 95% and 90% or 85%, individual physicians in their practice would not notice the difference because a vast majority of their patients would be cured. Well-conducted prospective clinical trials are needed to make sure that when we minimize treatment, we don't compromise the efficacy of the treatment and the success rate.

The treatment with ABVD alone has been tried in a trial in Canada for early-stage, favorable Hodgkin's disease. And we know that when we compare treatment with six courses of ABVD alone to the treatment with a shorter amount of ABVD and radiation or radiation alone, there's a slightly lower control rate. So patients treated with ABVD alone in our trial had a 13% risk of recurrence versus patients who had addition of radiotherapy, who had only a less than 6% risk of recurrence.

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DR. GOSPODAROWICZ: In addition, although ABVD chemotherapy is well-tolerated and does not appear to have any late effects, we know that Adriamycin® or doxorubicin – Adriamycin for A – does affect the heart. In some trials of patients with lymphoma rather than Hodgkin’s disease that were conducted in France, when patients were very carefully followed several years after treatment with Adriamycin-containing chemotherapy, there was noted an effect on the heart, although not a higher death rate.

The ABVD chemotherapy has been used extensively in the world now for over 20 years, but we still don’t have as good data on the long-term side effects of chemotherapy as we have on the long-term side effects of radiation. We need to continue studying the impact of our Hodgkin’s disease treatment on patients, not only focusing on the outcomes, on 5-year survival, 5-year outcome, but making sure that we follow patients and have population-based data that extend 20 and 30 years, to make sure that we, while trying to cure Hodgkin’s disease, don’t do any harm.

There are other new experimental forms of treatment for Hodgkin’s disease. There is a large amount of research going on to try to devise immunotherapy, probably anti-CD30 targeted monoclonal antibodies. These treatments are highly experimental. They’re not in clinical practice right now.

Now I’d like to say at the end just a few words about the lymphocyte predominant Hodgkin lymphoma. I said at the beginning that it’s slightly different disease. It’s a very distinct type. Almost 80% of patients with lymphocyte predominant nodular Hodgkin lymphoma present with Stage 1 disease, they present with a single lymph node. It is felt at the present time that involved field radiation alone is probably enough treatment for these patients. Although these patients do respond to chemotherapy, they tend to recur more often after chemotherapy. This form of Hodgkin lymphoma is associated with a close to 100% long-term survival rate, and one has to probably minimize the treatment in this group of patients. Because when there were large international trials of this disease conducted, there was concern that more patients may actually die as a result of complications of treatment in this disease than from the disease itself. So this is a very indolent form of Hodgkin lymphoma, where caution needs to be exercised not to over-treat.

That’s probably all that I would like to say at this moment and I’d like to open the session for questions.

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PEYTON MASON: Thank you so much, Dr. Gospodarowicz, for your presentation. Before we open up the lines and get to our interactive part of the program, I wanted to share some information with all of you on the line about a new program that The Leukemia & Lymphoma Society has just launched, our *Co-pay Assistance Program*. This new program offers financial support toward the cost of insurance co-payments and insurance premium costs for prescription drugs.

The program is currently open to patients with myeloma, lymphoma, including Hodgkin's, and acute myelogenous leukemia. Through this program the Society will provide financial support for patients whose income is at or within 400% above the federal poverty level. For more information on this program you can visit www.lls.org/copay or call the 877-number, and that's 877-LLS-COPAY. Of course, you can also call our Information Resource Center and get more information from them. That number is 800-955-4572.

We will now open up the lines to the question-and-answer session. Before the operator gives instructions for the audience to enter the question-and-answer queue, I would like to remind all of you that we do have close to 1,000 participants on the line and for everyone to benefit, please try to keep your questions general in nature and Dr. Gospodarowicz will provide an answer general in nature. Your phone line will be muted after you ask your question, so that the doctor can respond.

Operator, will you please give instructions to our teleconference participants so that they can queue themselves to ask a question.

OPERATOR: To participate in the call by asking a question, please dial star-1 on your keypad. We will take questions in the order that they are asked. Please be aware that due to time constraints, we can only take one question per person. Once your initial question has been voiced, the operator will transfer you back into the audience line. Again, to participate in the call by asking a question, please dial star-1 on your keypad.

Our first caller is Ed from New York.

ED: Just a general question. I have a friend who's 21 years old who has refractory Hodgkin lymphoma. He's had an auto-stem cell transplant and then had an allo-stem cell transplant using a matched sibling donor and then proceeded to have another recurrence. So right now he's on some type of maintenance drug therapy, he wasn't sure what the name was, but he has had two stem cell transplants.

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ED: I just wanted to know if there were any clinical trials going on that you might be able to recommend or any questions he might be able to ask his treating physician.

DR. GOSPODAROWICZ: I think that the management of Hodgkin lymphoma that failed two transplants is, as you say, best on clinical trials. I'm sure his physician has accessed the clinical trials inventory that's put out by the National Cancer Institute.

Also, if the patient is in New York, there are a number of cancer centers that will be able to direct the patient to the right clinical trial.

The problem with talking online like this about clinical trials is that the eligibility criteria for trials vary greatly, depending on previous treatment, the timelines and the patient's condition. But in this situation the trial of Phase I or Phase II new drugs is usually recommended. If the patient is not eligible for clinical trials, occasionally radiation therapy is used to temporize the disease, even in a young patient who failed all the other forms of treatment. That can stabilize Hodgkin's disease and offer a very good quality of life for a period of time.

PEYTON MASON: Thank you, Dr. Gospodarowicz, and thank you for calling on behalf of your friend. And just to let you know our Information Resource Center, all the specialists in the center are trained to provide assistance with a clinical trial search, a comprehensive search and to assist any patients or caregivers with figuring out if the trial is right for the patient. So please do call if you need any assistance with that.

We'll take our next question, please.

OPERATOR: The next question is from Amy in Pennsylvania.

AMY: Could you please talk about your approach to treating recurrent disease after multiple relapses of radiation and chemo in a 70-year-old woman?

DR. GOSPODAROWICZ: That's difficult because 70-year-old patient, when you don't tolerate bone marrow transplant very well, same advice as for previous patient. If there are clinical trials that the patient is eligible for, that may be the best avenue for further treatment. Again, treatment in this situation needs to be highly individualized. The aim is improve quality of life, maintain the quality of life. There is no known cure for patients who failed full courses of chemotherapy and radiation or failed the transplant.

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PEYTON MASON: Thank you, Amy, for your question. We'll take our next question, please.

OPERATOR: The next question is from Kenneth in Ontario.

KENNETH: Yes, doctor, I'm a male, 59, mixed cellularity, Stage 2. I had four cycles of ABVD, followed by three weeks of low radiation at Sunnybrook. I had a side effect, a bleomycin toxicity, resulted in a lung granuloma, small inflammation of the lungs. Was treated with an aerosol steroid, Advair®, for about six months.

My question is this. Other than the side effects, are there side effects to the cardiovascular system? More specifically, to any inflammation or clogging of the arteries. Since six months after I got rid of the granuloma, I found that I had a 90% occlusion in the left descending artery, which precipitated putting a stent in. And now this is six months later again, having difficulty breathing, and the cardiologist saying it's not heart and lung. People are saying it's not lung. I've had a follow-up CAT scan and the lung is clean of granuloma and everything else. So I guess my question again is, I'll be very simple, inflammation or clogging of the arteries as a side effect of bleomycin?

DR. GOSPODAROWICZ: That's not a usual side effect of bleomycin; however, the combination of ABVD and radiation does result in slightly more cardiac events. Now at the age of 59 it is possible that that could have been preexisting narrowing of the arteries, and the treatment could have exacerbated that or accelerated the atherosclerosing stenosis.

So, yes, definitely, there are side effects of combined modality therapy on the cardiovascular system. I'm glad you were managed very well with stenting. I'm sure your physicians will follow-up and try to diagnose the shortness of breath and manage you appropriately.

PEYTON MASON: Thank you, Kenneth, for your question. We'll take our next question, please.

OPERATOR: The next question is from Brett in Indiana.

BRETT: I'm a 43-year-old male with lymphocyte predominant Hodgkin lymphoma. I went through four cycles of ABVD and am trying to decide, since mine is close to the heart, if technology or studies have shown that radiation is not necessary. Or, if I do it, will the outcome be the same as if I don't. I've been to two different oncologists and radiologists, and it's a coin flip. I'm just wondering if there was anything you had studied or heard likewise.

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DR. GOSPODAROWICZ: So yes, lymphocyte predominant Hodgkin lymphoma. Our standard policy and practice guidelines suggest that patients are best treated with a combination of chemotherapy and radiation, although chemotherapy alone can be used. Four cycles is probably not enough. Current radiation techniques call for a lower dose of radiation and also for what we call involved field radiation, using IMRT, intensity modulated radiation therapy. I think you should ask about it. You should explore the centers that may tell you whether you can have radiation without affecting the heart excessively. It is uncommon for lymphocyte predominant to be lower down by the heart, but the treatment needs to be individualized.

Because lymphocyte predominant Hodgkin lymphoma is so rare, it's less than 5% of all the lymphomas, Hodgkin lymphomas that have lymphocyte predominant presentation, and most of them are in the neck and under the arm, you know, if we look at worldwide experience, it's probably very limited when looking for patients who have disease close to the heart. So, no, there won't be any specific data for your presentation. You really need to talk to your physicians to apply some general principles of lowering the exposure and maximizing efficacy of treatment.

PEYTON MASON: Thank you, Doctor, for that answer, and thank you, Brett, for your question. We'll take our next question, please.

OPERATOR: Your next question is from Kim in Virginia.

KIM: I have a son who is 7 years old. He just turned 7 and he was diagnosed with lymphocyte predominant, stage 1A. And he went through ABVE-PC and only had to have four cycles of it. And after the first cycle most of the cancer was already gone. He started off having about 5 centimeters removed via surgery and then he still had 10 centimeters of bulky disease. So he responded very well with the treatment, but now we've done a little bit of research, enough to be a little bit dangerous, and saw about the problems with the recurring cancers. He's only 7. So we're sitting back and wondering are there other cancers that we need to be worried about, that particularly strike people who have gone through lymphocyte predominant.

DR. GOSPODAROWICZ: I am not really an expert in pediatric Hodgkin lymphoma. I think that children with Hodgkin lymphoma are treated on a Children's Oncology Group study protocol and they have very well-defined outcomes. There is no doubt that any patient who has been exposed to chemotherapy or radiation therapy is at a higher risk of a second cancer.

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DR. GOSPODAROWICZ: Sometimes the risk are very low. One is always concerned about the risk in children, and all children who are survivors of pediatric cancer are followed for their lifetime. As the knowledge becomes available, appropriate screening tests and appropriate monitoring are being done. My best advice to you is instead of worrying about it, make sure that the child is in a program that follows pediatric cancer survivors.

PEYTON MASON: Thank you, Dr. Gospodarowicz, and thank you for your question. Just to bring you to some more resources from The Leukemia & Lymphoma Society, we do have an education series specifically for childhood cancer survivors, a telephone education program that's archived on our Web site.

First, the program of this year's series was *Childhood Leukemia and Lymphoma: New Options for Treatment*, with Dr. Sima Jeha. That program is archived. You can go to www.lls.org/survivorship to access that information. We also have local initiatives for educational and long-term survivorship needs for childhood cancer survivors. So please call our Information Resource Center and we can connect you with your local chapter. Thank you for your question.

We'll take our next question, please.

OPERATOR: Your next question is from Brian in Arizona.

BRIAN: Hello, Doctor. You touched upon this a little bit in your previous answers, but my daughter is 12 years old, she just went through four cycles of chemo for Hodgkin lymphoma. And so now we're at the point where we need to decide whether to do the radiation or not. So the thing that we need the most is just information. You mentioned there was a Canadian trial that had some good information as far as the risk 13% versus 6%. Would you be able to tell me where I can get such information?

DR. GOSPODAROWICZ: The trial was a trial in adult Hodgkin lymphoma. My presentation was focused on adult Hodgkin lymphoma. Most of the children that are treated for Hodgkin lymphoma, as I mentioned, are on Children's Oncology Group protocols. I would consult your oncologist and make sure that the child's recommendation for treatment matches the Children's Oncology Group protocols. From my limited knowledge, most children are advised to have very low dose, limited field radiation, otherwise the chemotherapy alone – the risk of relapse has been shown in the pediatric clinical trials to be higher. But you can get this information from your oncologist. As I say, I don't treat children with Hodgkin lymphoma.

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PEYTON MASON: Thank you, Brian, for your question. We'll take our next question, please.

OPERATOR: Your next question comes from Evelyn in Montana.

EVELYN: My son is 33 years old, and he had a relapse. He's been on this for two years. He went through the Stanford 5 series on the very first one and then his own stem cell transplant, which lasted six months. And now they have him on an antibody, the SGN-30. What would be the next course? Would it be a donor stem cell, or could he do the radiation? He looks good, he feels great, but there's still some active, I guess, in his lung.

DR. GOSPODAROWICZ: First of all, I'm sorry that he has recurred. As I tried to mention, unfortunately, we still have a number of patients who do recur after primary treatment. And the fact that the majority are cured doesn't help the patients and families who deal with recurrent disease.

I cannot really comment on the next step of management in patients who recur because most patients who recur after primary treatment and after stem cell transplant, need individualized approach to treatment. So it depends on where the disease is, what was the prior treatment, what was the response to the prior treatment, how long the disease has been going on. Certainly if radiation has not been used in the past in the area where there's difficulty now, it may be an option. Again, it has to be individualized.

PEYTON MASON: Thank you, Evelyn, for your question. We definitely are there for you on the national level by calling the Information Resource Center, and we'd be happy to provide you with information and also local support. We'll take our next question, please.

OPERATOR: Your next question is from Charmin in Nova Scotia.

CHARMIN: I have a 27-year-old daughter who failed two lines of chemo. She had a stem cell transplant one year ago in May. She followed that with 20 radiation, which was finished last August. Her original tumor was in her chest, it was 15 centimeters by 9, and it was nodular sclerosis, Stage 2B. I want to know what we can expect to see in our future CT scans, will the mass change size from the radiation that she's had or scarring? And what kind of time period? Thank you.

DR. GOSPODAROWICZ: So the treatment with stem cell transplant and I would understand that she had adjuvant radiation around the transplant, is effective. One would expect a certain decrease or resolution of any mass. As I mentioned, in nodular sclerosing, a persistent mass can be present.

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DR. GOSPODAROWICZ: And one has to monitor it and make sure it reduces in size and certainly there's no progression of growth. The most important time period after salvage treatment is the first two years. A relapse can occur later if the disease is not controlled. But it's very uncommon after five years or so. So the next couple of years or three, four years are very important, and I'm sure that the physicians who were involved in treatment are following the patient very closely.

PEYTON MASON: Thank you for your question. We'll take another question, please.

OPERATOR: Your next question is from Michael in Florida.

MICHAEL: I'm Michael's mom and I was wondering about in South Florida now there's a \$19 million proton therapy machine at Broward General. I would like the opinion about that machine for radiation.

DR. GOSPODAROWICZ: Proton radiation therapy is used selectively in some malignancies. It is used in children. I am not familiar with the South Florida facility. I think that you would need to consult your local physicians. There is no evidence right now that proton therapy gives much better results than regular gamma therapy, the high-energy X-rays. But depending on individual situation, there may be an opportunity to minimize the exposure of normal tissues, depending where the radiation is applied. So, I'm sorry, but I'm unable to comment on an individual situation.

PEYTON MASON: Thank you for bringing that question in on behalf of Michael. Again, this does bring up, very important for you to take the information that you learn today back to your healthcare team and to ask more specific questions to your healthcare provider. Hopefully this information will assist you with being informed to really be able to focus in on what's important to you specifically for your local needs.

We'll take our next question, please.

OPERATOR: Your next question is from Pamela in Alaska.

PAMELA: Hello, Doctor. I have a question concerning treatment. I'm 48 years old. I was first diagnosed with Hodgkin lymphoma in 2001. An extreme case of Stage 3B. I had ABVD. I had three reoccurrences, underwent an autologous stem cell transplant in February of 2004. I've had a hard time getting back on my feet. Just a lot of weakness and neuropathy type things.

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PAMELA: I wonder if there is any study going on for something nutritionally based or of the naturopathic or holistic type of treatment that's being studied or showing any success rate. It seems that with lymphoma being so tied to the immune system and the lymph nodes, that there would be something of a more natural way to successfully treat this. I still have two spots on PET scan that have been there since before the stem cell transplant, that still light up on the PET scan, so nobody will ever tell me that I am in remission. They just keep an eye on it to see if it's staying under control. The places are in the mediastinum, which was my original place to show up, and also in the thyroid area. And could that thyroid spot literally be just multiple cases of CAT scans and PET scans with the radioactive glucoses?

DR. GOSPODAROWICZ: So several questions. The role of alternative therapies. Certainly there's nothing against the normal vitamins, multivitamins. No other alternative therapy has been known to effectively re-boost the immune system and have effect on Hodgkin's disease. So your treatment was correct.

Time is a very good doctor and very good medicine for patients who undergo extensive therapy. And we find that a number of cases, the longer it is from therapy, whether it's combined modality therapy, whether it's transplant, patients regain energy and have fewer side effects.

As far as the risk of recurrence with PET scan that is positive, in the individual case I cannot comment. But PET scans are not 100% accurate. We do know that there are false-positive PET scans, especially small areas. Your physicians are quite correct to observe the area and if it's not changing, not to intervene. Just because the PET scan shows something, does not necessarily mean that it's unequivocal evidence of malignancy, especially if it's not progressing.

PEYTON MASON: Thank you, Dr. Gospodarowicz, and thank you, Pamela, for your question. We do have at The Leukemia & Lymphoma Society a fact sheet on integrative medicine and complementary and alternative therapies as part of blood cancer care. So please do request that fact sheet from our Information Resource Center for more information.

Now I would like to thank all of you for being on the line today. Our one hour program has come to a close. And please help me thank again Dr. Gospodarowicz. We are very grateful that she has donated this time to us today. We thank you for all of the work that you do today in supporting families touched by lymphoma.

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PEYTON MASON:

We would also like to thank again everyone on the phone today. We appreciate that you have set aside this time to learn more about Hodgkin lymphoma. We hope that your questions were answered and that the information provided will assist you in your next steps.

And a reminder to all of you to fill out your program evaluation. If you're a nurse or social worker, fill out your continuing education credit form. Please return those forms in the envelope provided. Feedback is extremely important to us and it helps us plan the most meaningful programs for you, so your comments and suggestions are certainly appreciated.

And a reminder to all of you that our Information Resource Center is open. Please do not hesitate to contact us if you have further questions. Our Master's level information specialists are available to provide you with more information and can link you with your local chapter and support services. Again, that number is 800-955-4572. That number is included on the materials in your packet.

On behalf of The Leukemia & Lymphoma Society, I'd like to thank all of you for sharing this time with us today. Good-bye and we wish you well.

OPERATOR:

This concludes today's conference call. You may now disconnect.

END