TRANSCRIPT

Follow-Up Care for Blood Cancer Survivors: The Critical Role of Primary Care Providers

Robert J. Arceci, MD, PhD
Judith E. Karp, MD
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Slide 1: Follow-Up Care for Blood Cancer Survivors

Anita Welborn:

Hello, everyone. My name is Anita Welborn and I am the Vice President of Patient Services Operations for The Leukemia & Lymphoma Society. On behalf of The Leukemia & Lymphoma Society, allow me to welcome you and thank you for choosing to spend this hour and a half with us today for our program *Follow-Up Care for Blood Cancer Survivors: The Critical Role of Primary Care Providers*, featuring Dr. Robert Arceci and Dr. Judith Karp. We thank our speakers for sharing their time and expertise with us and for their dedication to serving families touched by cancer.

We would also like to acknowledge and thank Genentech and Biogen Idec for their support of today's program.

Before I turn the program over to our speakers, I would like to remind you that The Leukemia & Lymphoma Society is committed to bringing you the most up-to-date information about blood cancers, so you can stay current in your field and help patients get the best outcomes.

Our vision is that one day the great majority of people who have been diagnosed with a blood cancer will be cured or they will manage their illness with a good quality of life.

Since its founding in 1949, The Leukemia & Lymphoma Society has invested more than $680 million for research specifically targeting blood cancers. We will continue to invest in research for cures, programs and services that improve the quality of life for patients and their families.

We hope this webcast will be helpful to you with your work and support of patients.

Slide 2: Robert J. Arceci, MD, PhD & Judith E. Karp, MD

I now have the pleasure of introducing our speakers and then we'll get started with the program.

Dr. Robert Arceci is the King Fahd Professor of Pediatric Oncology and Professor of Oncology and Pediatrics at the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins in Baltimore, Maryland. After receiving his medical degree and doctorate from the University of Rochester in New York, Dr. Arceci went on to complete his residency and fellowship training in pediatrics and pediatric hematology/oncology at the Children's Hospital and Harvard Medical School in Boston, Massachusetts. Before joining the staff at Johns Hopkins, he held faculty appointments at Harvard Medical School, Boston Children's Hospital and the Dana-Farber Cancer Institute. Dr. Arceci's research focuses on translational research in pediatric malignancies and serious blood disorders, as well as on optimizing comprehensive care for children and adolescents with cancer. He has been particularly involved in the development of novel therapeutic targets and immunotherapies while reducing adverse side effects in patients with cancer. Dr. Arceci is considered an international authority in many challenging clinical pediatric oncology areas

including the diagnosis and treatment of leukemia and Langerhans cell histiocytosis. He is editor-in-chief of *Pediatric Blood & Cancer* and also serves as associate editor of the *Journal of Pediatrics*.

Along with Dr. Arceci, we have Dr. Judith E. Karp. Dr. Karp is a Professor of Oncology and Medicine and Director of the Leukemia Program at the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins Hospital in Baltimore, Maryland. She received her medical degree from Stanford University School of Medicine, completed an internship and residency at Stanford University Hospital and Johns Hopkins Hospital, and completed her oncology fellowship at the Johns Hopkins University School of Medicine. Her research interest focuses on the experimental therapeutics of acute leukemias, including development of time-sequential therapy, new biologic agents for older adults with acute leukemias, and new approaches to the treatment of refractory acute leukemias including secondary leukemias that evolve from myelodysplasia or from prior cytotoxic chemotherapy. Dr. Karp has been an active member of The Leukemia & Lymphoma Society's medical and scientific affairs committee since 1995 and served as vice-chair for clinical research from 1998 through 2002. Dr. Karp was instrumental in the development of LLS grant programs including the translational research program and the Scholar Award in clinical research. She also received the prestigious Dr. John J. Kenny Award from The Leukemia & Lymphoma Society in 2007.

It is my absolute pleasure to turn the program over to our esteemed speakers. Dr. Karp and Dr. Arceci, we are honored to have you here with us today.

Slide 3: Disclosures

Dr. Judith Karp:

Thank you so much, Anita. This is a great privilege for us as well.

And I believe it's fair to say that neither Dr. Arceci nor I have anything to disclose other than our good intentions.

So let's get started with our lecture.

Slide 4: Scope of the Issue

The first thing that we'd like to do is to set the stage for you in terms of just how important are blood cancers in the scope of all cancers. And I think you will see from this slide that the incidence and the deaths from blood cancers are certainly not trivial. In the year 2009-2010, there's an expected total of 1.5 million cancers that will be diagnosed and 560,000 patients will lose their lives to cancer.

Lung cancer remains the greatest incidence and death rate. Breast cancer is next in terms of incidence, 190,000 diagnoses per year, but only 40,000 deaths per year. If you take the blood cancers, they have the same incidence and death rate as colorectal cancer, so that's not small. In addition, when you look at pancreatic cancer alone, the incidence is expected to be 42,000 newly diagnosed patients this year and 35,000 deaths.

So the truth is that blood cancers are about 10 percent of all cancers, both in incidence and deaths, and that does not include myelodysplasia, which is clearly a myeloid malignancy as well. So even without myelodysplasia, there are now almost a million people surviving with blood cancers in the United States today.

Slide 5: Survivors of Childhood Cancer

Now in our next slide, the greatest, most rewarding perhaps data, come from the survivorship in childhood cancer, where 85 percent or so of young children are enjoying at least a five year survival. This is major progress in the last few decades. We should be so lucky with adults. We are not yet, but we're

coming along slowly. However, this survivorship is not without its challenges and that's what we're here to discuss today.

Slide 6: Gender-Specific Survival

The next two slides will be a series of beloved Kaplan-Meier curves and I'll try to summarize them and put them into English. I think that the important thing is that cancer has a long-term impact on both the length and the quality of life. There are some differential effects between men and woman and, as you'll see in subsequent slides, differential effects in terms of the different types of cancers, the therapies and the long-term complications.

Slide 7: Disease-Specific Survival

In the next slide, I told you the next two slides, what you'll see is the overall expected survival for children who have various types of malignancies. And again, different primary tumors have different impacts on the overall survival and it relates both to the tumor itself and to the type of therapy.

Slide 8: Disease-Specific Survival

The next slide is just a continuation of that.

Slide 9: Cumulative Cause-Specific Mortality

And then slide number 9 gives us a different viewpoint. I think the important message here is that the risk of complications extends long after the initial diagnosis and therapy. The occurrence of a secondary malignancy, a tragic and ironic event, is second only to recurrence of the original leukemia in terms of its incidence over time.

Slide 10: Case Study #1

Now we're going to give you some examples and specifics regarding this. And in the next slide we present very briefly for you an 18-year-old female who had stage III Hodgkin lymphoma. She was treated with combination chemotherapy along with low dose mediastinal radiation and obtained a complete response. During the therapy, because of the steroids, she developed osteonecrosis. The therapy was completed within a six to eight month period of time, however, two years after she stopped therapy she developed restrictive lung disease and finally nine years after stopping therapy, she developed right-sided breast cancer in the radiation field. This is tragic, but not unheard of and not uncommon.

Slide 11: Breast Cancer in Hodgkin Lymphoma Survivors

And the next slide will show you how much of an incidence there is of the development of breast cancer in adolescents and young women who have Hodgkin disease and who receive chemotherapy and in particular radiation. This is early onset breast cancer. The overall incidence is remarkably high. And we think that this is attributable to the effect of radiation on highly proliferative breast tissue that increases this risk.

Slide 12: Case Study #2

Now let's look at it from another point of view. Let's look at it from the point of view of an adult patient this time. You have to keep in mind that older patients are equally at risk for life-threatening complications. In this presentation we'll think about a 52-year-old lady who had stage II left-sided breast cancer. She had a mastectomy followed by six cycles of dose-dense chemotherapy that included anthracyclines and growth factors. She then had chest wall radiation. She did well until four years later, when it was noted on routine examination that her blood counts had started to fall. And over the next several months, her physician noted progressive pancytopenia with fall in hematocrit, white count in particular, neutrophils and platelets. After three months or so, a bone marrow was obtained which showed characteristics of myelodysplasia with trilineage dysplasia of the erythroid, myeloid, and megakaryocytic lines. And in addition, karyotypes were obtained and she was found to have complex cytogenetics. Over the next few months this myelodysplastic syndrome evolved into a full blown AML. She then underwent intensive chemotherapy, including anthracycline, for her AML. She did not achieve a complete remission, but tragically her left ventricular ejection fraction dropped precipitously and she was left with a cardiomyopathy.

Slide 13: Late Complications of Therapy

Next slide. So with the next few slides we're just going to go through the causes and manifestations of the late complications of therapy for hematologic malignancies.

The treatments are systemic and that means that multiple organ systems are at risk. The types of complications depend on the type of therapy, specifically the types of drugs or immunotherapy. For instance, following bone marrow transplantation. And some of the complications also reflect the underlying disease itself, for instance, iron overload.

And what I present for you here is the organ system that is affected, the types of agents that can cause the organ system problem and what those clinical manifestations are. And as you can see, virtually all of the important organ systems are affected. Cardiac pulmonary,

Slide 14: Late Complications of Therapy

Renal, endocrine and reproductive, hepatic.

Slide 15: Late Complications of Therapy

Neurologic, the bone and musculoskeletal system, and the immune system. I think you can review all of those at your leisure.

Slide 16: Secondary Malignancies

What we're going to talk about briefly now are the secondary malignancies that are late complications of therapy for blood cancers.

This is a great irony. It's, if you will, the price of our success. And it's something that was not recognized until 1980 when the survivors of Hodgkin disease treatment were now developing secondary leukemias. And this was a very important discovery. And up to 10 percent of patients with stage IV Hodgkin disease, who are cured of their Hodgkin disease, will have treatment-related AML.

And there are two culprits here. There are the cytotoxic drugs, which cause myelodysplasia or leukemia, and then there are other malignancies as well. The radiation, as we already talked about, can

cause breast cancer. Central nervous system radiation can be responsible for brain tumors, in particular meningiomas, which are histologically benign, but clinically not necessarily so. Sarcomas and bone tumors, skin cancers and thyroid cancer. And these are life-long risks.

Slide 17: Long-Term Complications of Steroids

Another class of drugs that are used frequently in the blood cancers are steroids. And while many people will say oh, the cytotoxic drugs, the alkylators or the nucleoside analogues, those are the really terrible drugs, steroids may be among the most dangerous drugs that we use, because we use them at high dose and for long-term and because we underestimate their potency in terms of long-term consequences.

And these long-term consequences affect individuals at all ages. Obesity, diabetes, osteonecrosis, as in our first case presentation, relative adrenal insufficiency, alternatively hypertension and major psychological disturbances.

Slide 18: Psychological Impact of Survivorship

In that regard, last, but not least, the complications of being a cancer survivor are not relegated to physical issues alone. There is a huge impact psychologically and I think we under-appreciate that at all times, and this, too, is a lifelong impact. There is survival anxiety. The other side of that is that people are very glad to be alive, and that is very rewarding, but that doesn't happen to everybody. The so-called chemo brain may not last forever, but it seems like it lasts forever. Chronic fatigue, body image, and then worry about one's offspring. Will those offspring have cancer as well?

So this is an introduction to Dr. Arceci, who's going to give you some very detailed descriptions related to survival in these patients.

Dr. Arceci?

Slide 19: Key Elements of Survivorship

Dr. Robert Arceci:

Okay, thank you, Judy.

I will now just pull up this next slide here and try to impart to you some of the landmark findings of a profound national effort that has been through the Children's Oncology Group as well as through many institutions throughout the country, looking at large, large numbers of survivors of childhood cancer, childhood and young adult cancers. And this work was published by Dr. Oeffinger et al and Les Robison, the senior author on this particular paper, has been involved with cancer survivorship for many, many years. And currently he's at St. Jude's and Dr. Oeffinger is at Memorial Sloan-Kettering.

Now the importance of this initial study, and there have been many smaller studies before this and I'm just focusing on this one because of its depth and numbers, but this group looked at close to 10,400 survivors and very importantly looked at about 3,000 siblings, so it was a very important control group there. Another key element to this study, which it has been criticized for at some level, is that these are patients who were all treated before 1986. And you could say that in fact we're so much better at doing this now than we were then, that I'm sure we won't have any problems with survivorship issues in the future, but that is, I can tell you, certainly not the case. But there may be some new things that happen with the way we're treating patients currently.

So what that did was to determine through surveys the frequency of chronic conditions, the severity of those conditions and the relative risks of those chronic conditions as the result of either disease or treatment.

Slide 20: Childhood Cancer Survivorship Findings

The next slide that is coming up now has to do with the findings of that trial. The age range, the average age of the survivors that were looked at was about 27 years of age. The average range of siblings was about 29, so pretty close. And the time from cancer diagnosis to survey, the average was about 17.5 years. So this is long-term follow-up now and they had a superb effort in that regard. Forty-six percent of these patients were women. And unfortunately or fortunately, I guess, only 16 percent were minority groups, so you have to keep in mind that there may be differences in subgroups of survivors. But we just don't have these kinds of numbers in all of the groups. We'll look at that a little bit more in a second.

Slide 21: Childhood Cancer Survivorship Findings

The next slide, 60 percent of these survivors had at least one chronic condition identified, not necessarily life-threatening, but a chronic condition that needed medical attention; 25 percent had a severe or life-threatening condition. And by severe it meant that it resulted in a disability. And about 40 percent of all these survivors had two or more and 25 percent had three or more chronic healthcare conditions. So we're going to go back to these numbers in a little while to give you a different appraisal of what survivorship really might mean.

Slide 22: Relative Risk: Survivors vs. Siblings

Now the next slide coming up has to do with looking in a little bit more granularity at the differences of side effects between survivors relative to the siblings. As you can see on the top line here, major joint replacement, this has mostly to do with patients who have had bone tumors, but also a significant number who have suffered osteonecrosis, as that first patient that Judy discussed. Congestive heart failure is 15-fold relative risk, compared to their sibs. This is completely not trivial, of course. Secondary malignancies, 15-fold. If you keep going down this, cognitive dysfunction is quite significant relative to their siblings. And the severity of these is quite variable. But as you go down this list here you can see almost every single organ affected, including issues like coronary artery disease, possibly high and because of radiation, mediastinal radiation, we know that as a particular risk factor. A lot of the drugs that we use that are curative affect hearing, which affects speech, which affects a lot of the quality of life issues. And there are in fact patients who are legally blind as a result of their treatment and/or the disease. And of course, the fertility issues that are evident.

Slide 23: Relative Risk, cont.

Now on the next slide you can see that these findings were placed in terms of relative risks and again, 3.3 times greater of survivors than their sibs to have a chronic condition, 8-fold more for survivors than sibs to have a severe life-threatening condition, which is enormous, and then the relative risk of having two or more of any of the above was about 5 times more than their siblings.

Slide 24: Cumulative Incidence of Long-Term Effects

Let me just move on here to the next slide. Again, the cumulative incidence here is 73 percent of a problem. Those can be mild to severe. And the incidence of a disabling or life-threatening condition could be as high as 42 percent in this cohort, which is an incredible number in so many ways.

Slide 25: High Risk Groups: Diagnosis

Now if you look at the next slide and some of the types of diseases that result in differences in the relative risk of developing I to IV grade, I to IV, or in fact grade III to IV, that is life-threatening or disabling conditions, and just focus on the asterisked diseases like Hodgkin disease, non-Hodgkin lymphoma and leukemia, the ones that we're relatively talking about today, you can see here that these are non-trivial as well. Five-fold risk of the patient survivors versus their siblings in terms of grade I to IV for patients with Hodgkin lymphoma; severe side effects or adverse sequelae, 10-fold greater. And then if you look down here at non-Hodgkin lymphoma, relatively similar values, and under leukemia, although somewhat smaller and this may have a lot to do with the fact that a large number of these patients were survivors of childhood ALL, which we've learned that we can treat much less intensely than certainly for myeloid leukemia or adolescent or adult ALL.

Some of these adverse sequelae for leukemia, however, is in a period of time where if a patient presented with significant central nervous system leukemia, then they almost always received cranial radiation. We'll get back to that topic in a little bit.

Slide 26: High Risk Groups: Treatment

The next slide looks again at some of the details of the types of relative risks. If you had any chemotherapy, alkylating agents, as Judy said, in terms of secondary leukemias here, anthracyclines in terms of the risk of heart disease, radiation treatment, particularly if you've received central nervous system radiation, can result in quite significant relative risk of grade III or IV adverse sequelae. Chest irradiation in terms of pulmonary function as well as coronary artery disease. And pelvic irradiation in terms of potential issues of fertility and secondary tumors. And on the bottom here is surgical issues regarding nephrectomy, which really are not part of what we're talking about today.

Slide 27: High Risk Groups: Treatment

The next slide extends that analysis now to looking at specific regions. If you look at chest radiation, you can see a 14-fold incidence of developing a grade III or IV toxicity. Bleomycin associated with significant adverse outcomes as well.

So any of these listed right here result in anywhere between roughly a 10- to 20-fold increase in quite severe toxicities.

Slide 28: Cumulative Incidence of Chronic Health Conditions

And when you look at these in aggregate on the next slide, you can see that this cumulative incidence does not seem to just disappear. Judy alluded to this earlier in her session on this, and any toxicity is in the range overall about 73 percent. And the chance of getting a grade III to V severity adverse sequelae rises into close to 40 percent over the average here was stopped at about 28 to 29 years. So the relative risks keep going. And this is something that is particularly important in terms of how these patients need to be followed by, of course, their primary care doctors, and how cancer centers need to relate to all of those people.

Slide 29: Major Problem Areas

Now the next slide has to do with major problems then in terms of the types of issues that we tend to see. The secondary malignancies are particularly problematic, as that slide Judy showed earlier.

Coronary disease, pulmonary fibrosis and endocrine problems. This goes along with children or adults.

Slide 30: Problems by Diagnosis

The next slide lists some of these other issues, particularly bone and brain tumors, the problems that are associated with those. But here today in terms of leukemias or Hodgkin lymphoma, particularly cardiovascular disease; secondary cancers are profoundly important; thyroid dysfunction and thyroid cancers, as Judy had mentioned.

Slide 31: Problems by Race and Age

The next slide, from my perspective here, just also addresses the issues of race. I alluded to this just a little bit earlier. This does not seem to be necessarily correlated in terms of the development of severe chronic conditions, however, Black, non-Hispanic survivors were more likely than Caucasians or White, non-Hispanic survivors, to develop some type of chronic condition.

And age is also an important issue. Not intuitive here, but the older aged patient, that is in the pediatric group, but there are specific issues for the adult as well, at the older ages, in fact more frequently associated with the development of any condition, severe or in fact multiple conditions. So the 5 year old, if treated with agents and cured, has less of a chance than a 15 year old or a 20 year old of developing one of these.

Now I'll leave this, send this back to Judy, and bring up the next slide, and she's going to deal with some of these details as well.

Slide 32: Timing of Chronic Conditions

Dr. Judith Karp:

Thank you, Bob.

So the next several slides are going to look in a little more detail at the timing of the types of chronic conditions that can emerge as sequelae of various blood cancer therapies.

And I think that this slide really says it all in some ways, which is that these problems can occur 20 or 25 years after the primary diagnosis and therapy. And the reason that we've stopped at 25 is we don't have enough people truly to evaluate what's going to happen in 40 or 50 years. And I think that that's something for the next generation of physicians to be very aware of, with very open eyes and open minds.

The highest incidence of chronic illness that accumulates with chronic changes over time, occurs in the setting of radiation therapy. Now whether this is radiation alone or chemotherapy plus radiation therapy, the onsets are really continuous over time. Chemotherapy conditions tend to occur earlier and plateau, whereas the radiation therapy changes are much more cumulative and progressive.

Slide 33: Timing of Chronic Conditions, cont.

On this slide, this article by Lisa Diller is really a spectacular article. It's in *Journal of Clinical Oncology* in 2009. It's really a fantastic article. And this slide depicts the different manifestations of chronic pulmonary disease either from chest radiation therapy or from pulmonary toxic chemotherapy such as bleomycin. Again, radiation may be the main cause of pulmonary fibrosis and symptomatic changes, but chemotherapy has additive effects clearly.

Slide 34: Timing of Secondary Cancers

Now another issue we have repeatedly discussed is on is the secondary malignancies. And here, this again depicts actually a slow cumulative incidence early on, with a really accelerated development in the period of time between 10 and 20 to 30 years after the primary malignancy.

And you'll see two curves here. One is all secondary malignancies and the other is non-melanoma skin cancer. And non-melanoma skin cancer has a significant incidence; it's not something that should be disregarded just because lots of people get basal cells and squamous cells from sun exposure. Sun exposure and radiation and chemotherapy all have the same effect on the skin organ.

Slide 35: Height Issues by Treatment

The next two slides deal with issues of height. These issues relate predominantly to radiation, but also you cannot forget about steroids as a major contributing factor. And the type of radiation or the location of radiation is important. Cranial irradiation gives you some significant decrement. Cranial-spinal irradiation gives you even more.

Slide 36: Height Issues by Diagnosis

And if you look at the next slide you will see that the height issues predominate in the acute leukemias and in the central nervous system tumors, relative to other tumors, and that makes a great deal of sense because these are the tumors, the central nervous system tumors, where there's lots and lots of radiation. In the acute leukemias, there's steroids and radiation. So this is something that one has to watch out for, particularly in children and young adolescents. Not so profound in young adults and older adults.

Slide 37: Height Issues and Growth Hormones

The next slide relates both to the height issues and to the notion of growth factors in general. This is a very controversial issue. Growth hormone has been used to stimulate growth, obviously, after chemotherapy and radiation therapy. And what I'd like to call your attention to in particular is the 5-fold increased relative risk of acute leukemia in patients who have had growth hormone from a previous malignancy. And that I think is controversial, but a very important thing to keep in mind.

Slide 38: Obesity

Obesity is another major problem and the problem may be greatest for children, but certainly adults are affected by this as well. And this is a linear relationship with steroid use, both the amount and the length of time.

Slide 39: Menarche

In the next slide, looking at age of onset of menarche in young children, the children who receive some type of radiation, and particularly cranial-spinal, so that they're having pelvic radiation, will actually have early menarche. The other side of this is in relatively young adults who can be thrown into early menopause from alkylating agents in particular, or radiation as well.

Slide 40: Osteonecrosis

Now my last slide, before I give this back to Bob, speaks to osteonecrosis. We've talked about this already. This is a major issue. It's important in children, but perhaps even more important in adults. It's a major issue in adults. It is linked almost exclusively with steroid use. And it doesn't appear to have any stopping point. Once you've had steroids for a malignancy, you are at risk, it would appear, for the rest of your life for osteonecrosis.

And now I'm going to hand it back to Bob.

Slide 41: Alternative Assessment of Survivorship

Dr. Robert Arceci:

Thank you, Judy.

What this all boils down to is I think a slightly different way to look at survivorship. And we talk about a 75 to almost 85 percent, "cure rate" in pediatric oncology now, but if you look at survivorship in terms of what really is happening, you can see that (and this is completely theoretical now at some level, but it's based upon data that we have seen and discussed) if you take a 75 percent cure rate and you subtract those who have one serious condition, you're down to 50 percent. If you take away 40 percent of those having two or greater serious conditions, you're down to 35 percent. And if you have at least one condition and you subtract your 66 percent roughly from your 75 percent, we're curing less than 10 percent of patients, if you really are talking about the cure, which we dreamed about certainly back in the 50s, when children first of all started to be treated with multiple chemotherapeutic agents for ALL and adults, of course, with nitrosoureas for Hodgkin and other types of lymphoma. So this doesn't detract from the fact that patients are surviving, but the issue now, of course, is that we would love to be able to say you can survive with the same level of security in terms of your health and welfare as those who have not experienced cancer. We aren't there yet. So it makes all of our jobs particularly important.

Slide 42: Barriers to Optimal Care

So how do we deal with all of these adverse sequelae and these patients who have them in terms of the problems, the potential problems, and actually the real problems?

First of all, everybody does talk about everybody needs more money to do these things, but survivorship issues have in the past been under-funded. There's little question about that. And certainly programs are not reimbursed as you would if you were taking out an appendix, for instance.

The standard methodologies to understand neurocognitive, psychological and physical well-being have not been very well developed and tested and validated. They are also not at every center and difficult to get.

In spite of recent legislation in this country, insurability remains an issue. I had a colleague here at Johns Hopkins, who came here to work as a physician, and was initially denied healthcare because she is a survivor of childhood leukemia. So she had leukemia when she was 5 or so years old and here she is, an adult coming to work as a physician, and denied healthcare insurance. So insurability, job discrimination, military service, all of these things are often difficult for survivors to achieve.

We do not yet, although it's developing rapidly now, at least in the pediatric world, have a true national database. And this is a rapidly evolving area.

And lastly, the issues of linking long-term care and survivorship issues to disease experts, and that is not just in the areas of people who are experts in AML or ALL or lymphomas, but also to those cardiologists, to those orthopedists who also have an appreciation for these diseases and their adverse sequelae.

And lastly, I think a tremendously important thing we have not yet achieved, is how we can link cancer care, long-term cancer survivorship issues, to primary care providers, noting that fewer than 20 percent of survivors are followed, for instance, at cancer centers. So that means a lot of people aren't being followed at cancer centers at all.

Slide 43: Survivor-Related Barriers

The next slide continues to look at this in a paper by Oeffinger in *Pediatric Blood & Cancer*, where this particular group looked at some of the individual barriers. And if you say, well, survivors shouldn't have any problems with their own healthcare, well, it's not quite that way. Most survivors, when they were surveyed, were not aware of their treatment details or the potential late effects associated with, number one, their treatments or their cancers. Thirty to 50 percent of these patients or survivors remember receiving anthracyclines in some form, but that means a lot don't have a clue that they actually received a cardiotoxic drug like that. And we've already gone over the incidence and relative risks of exposure to these agents, so that's quite significant. Only 70 percent recall the site that they were irradiated. Thirty-three percent were splenectomized and knew about it. Only 15 percent reported having received a summary of their cancer therapy, so 85 percent of cancer survivors don't really have a detailed history to provide to a primary care provider when they show up in the office. And of course, most of these patients do not have any knowledge of their family history in terms of some of these diseases and potential risks. And it's not just about the risk of cancer, it's your risk of heart disease in combination with your treatment for cancer. So if your family has a very high incidence of breast cancer, you can be assured that your risk may be even higher if you have been exposed to mutagenizing agents.

Slide 44: Physician-Related Barriers

Now doctors aren't perfect, even though sometimes we think we are, but we also have been blinded by some of these things. There is simply not enough of these long-term follow-up clinics and follow-up programs. Most of the programs, the ones that exist, do not follow survivors through adulthood. Ninety-six percent of pediatric oncologists will in fact follow patients for up to about five years, but only 52 percent for life, and that is probably appropriate, but the handoff here is what's terribly important.

There is a lack of, not dedicated nurses, but dedicated nursing staff focused on this problem, and they can be a tremendous help in partnership.

There's also been a lack of communication between cancer centers and primary care physicians regarding survivorship.

Slide 45: Healthcare System-Related Barriers

And lastly, there are, in fact, inherent system issues, that is coverage of healthcare systems and insurance companies beyond minor years. This is quite a major issue. And, of course, loss of work and loss of coverage. Most insurance coverage being often linked to your employment.

Slide 46: Summary of Barriers to Care

So this next slide I won't go over in detail, but it's a summary of the data from this particular manuscript. And it really looks at the details of survivor barriers, healthcare system barriers and the knowledge of physicians and healthcare professionals, all of which contribute to either optimal or less than optimal long-term care.

Slide 47: Survivorship: Problems & Solutions

The next slide now talks about survivorship problems and some of the solutions. There's a golden rule that if you have a problem you should in fact come up with a solution if you're going to present it. Since the Institute of Medicine's report on cancer survivorship, there has been more interest at NIH. And in terms of insurance companies, they have started to get involved in this, as well as groups like ASCO and American Association for Cancer Research.

There are standard methodologies that are needed and they are being developed. These other areas of insurability and job discrimination are being addressed, but not at necessarily a truly effective national level. We'll talk a little bit about these last two points in a second.

Slide 48: Essential Elements of Survivorship Care

The next slide has summarized the issues of the key elements of survivorship monitoring and that is knowing how to do surveillance of these patients, knowing how to intervene. This is what happens in I'm sure the primary care providers' office all the time for all their patients, but for this group they're at particularly high risk. To develop interventional strategies. And then a major issue, of course, is how do you coordinate all of this complex care? It is not trivial and it is very time-consuming.

Slide 49: Risk-Directed Screening and Care

The next slide starts to look at some potential areas that can be of service to those providing care for these survivors. Number one is a set of guidelines, and we'll go over just a few of those very quickly, but this particular website, Survivorshipguidelines.org, which are a set of guidelines developed through a consensus committee, evidence-based guidelines from the Children's Oncology Group, but they are quite relevant no matter how young or old you are.

The Passport for Care, which was developed initially at Texas Children's Center, but other centers have done similar types of things, are basically to have your past history and exposure and risk, either on a CD-ROM, a memory stick, and of course, having it available online, that is protected, but then if a patient does show up in your office, you would have the ability to access this history.

And then the issues of prevention counseling, education and intervention.

Slide 50: Biology and Predispositions

We have developed here at Johns Hopkins, with the help of the Garil family, an approach through the Michael Garil Leukemia Survivors Program, a slightly different approach, based upon predisposition and trying to understand both the biology and the related risks of who is at particularly high risk for developing specific changes or specific adverse sequelae.

Slide 51: Biology and Predispositions

This particular website is available throughout anywhere in the world and you're welcome to log onto this and send questions as well.

Slide 52: Survivorship Guidelines

The guidelines, I wanted to go over a few of those right now as well. The Survivorship Guidelines through CureSearch and the Children's Oncology Group are quite extensive.

This is the website. It's incredibly easy and fast to go onto. You just put this in your web browser and then you immediately can either download the entire file through a PDF or you can go online and do this.

Slide 53: CureSearch

And you can see here a list of various areas to click on.

Slide 54: CureSearch, cont.

So if you look down this list you can see introduction to long-term follow-up, this is both in English and in Spanish, and other languages hopefully will be coming online. But you can follow risks for cataracts, healthcare, pulmonary health, bleomycin alerts, Raynaud's, chronic pain, all of these different areas. A simple click gets you into a screen that might look, for instance, like the following slide.

Slide 55: Example of Exposure and Follow-Up Recommendations

And on this particular slide here, you have an analysis of the issues associated with psychosocial disorders. And you can see here that they have potential late effects, risk factors, the highest risk factors, and they give you guidelines as to how frequently you should be doing what kind of surveillance.

Slide 56: Alkylating Agents and Fertility

The same type of approach is shown in the next slide in terms of exposure to alkylating agents. And importantly here, you have issues under periodic evaluation and the effects on fertility, how to monitor patients, how frequently you should be doing some of these screening approaches.

Slide 57: Alkylating Agents and Secondary Malignancies

If you look on the next slide you can also see the risks of hematologic secondary malignancies like the patient Judy described initially, the second patient, the 52 year old woman who developed AML after therapy for breast cancer. And you can see here how to monitor these. And at the bottom you can see that all of these guidelines are based on the best literature out there, so this group has done the work for us, which is an incredible resource.

Slide 58: Alkylating Agents and Renal Function

The next slide looks again at alkylating agents in terms of renal function and kidney function over time and exposure to things like ifosfamide may create renal wasting of certain metabolites and minerals for 10 to 20 years. And so the kidney remembers for a long, long time.

Slide 59: Anthracycline Exposure

On the next slide you can see the issues associated with anthracycline exposure and this can, of course, relate to secondary malignancies based on its mutagenesis properties, but also how you monitor patients.

Slide 60: Anthracycline Exposure

And what's important with a simple click, you can move on to the relative risks and how to monitor patients, based upon how much anthracycline they received and how old they were when they received it. So this type of information, when you see a patient who, if, of course, you know this, that they've had the exposure, leads you into an important way to follow them, that should be very straightforward.

Slide 61: Corticosteroid Exposure

And then lastly, Judy has talked extensively about the effects of corticosteroids and these have immense long-term issues in terms of bone density and mineral issues.

Slide 62: Breast Cancer Risk

And if you are interested, for instance, in the risk of breast cancer and what the exposures might be, you can just click on breast cancer and you can see here the risks of breast cancer, the high risk, any patient at risk, groups involved, as well as how you should periodically evaluate these patients and by what screening approaches.

So this is an incredibly important resource that's available worldwide to anybody, including patients. So you in fact, as the word gets out, may have patients coming to you with this and so you might as well be prepared, a priori.

I'm going to give it back to Judy in terms of finishing up with some comments on adult survivors.

Slide 63: Adult Survivors

Dr. Judith Karp:

Thank you, Bob.

I think it's important to keep in mind that while there are lots of, proportionately lots and lots of childhood survivors of childhood cancers and that those folks will grow up to be highly productive adults, adults themselves who develop cancer as adults are surviving in greater numbers, and the complications of our therapies are extremely important.

The adults who survive cancer that arises during adulthood have the same basic patterns as with children, but there are some age-related differences.

Adults who are adult survivors have increased risks for secondary leukemias, osteonecrosis, iron overload, chronic infection, chronic fatigue, depression and graft-versus-host disease in both acute and in particular chronic, following bone marrow transplantation. On the other hand, survivors of adult cancers and the therapies may actually have fewer lasting neurocognitive disorders and fertility issues.

Slide 64: Role of the Primary Physician

So the next question is how should we manage adult patients? And not just adult patients, but children as well, what is the role of the primary physician? Well, the primary physician for cancer survivors is really the patient's first line of defense. A careful serial history, physical examination and a detailed composite of all of the previous anti-cancer therapies, if you can get it: the names, the total doses, and as Bob said, the dates of administration and what were the conditions under which the drugs were administered.

An awareness of the complications that both Bob and I have been talking about: what are the target organs, when was the onset relative to when the therapy was administered, and what are the clinical manifestations?

Preemptive screening and follow-up: this I particularly important for things like breast cancer and osteonecrosis.

Prompt referral to the appropriate specialist.

And last, but not least, if you as the primary physician don't tell us, the oncologists, of these problems, we're not going to know about them. Now you can say well, why aren't you following your patients? Well, we may well follow our patients and hopefully we do follow our patients for this particular issue, but our expertise is not endocrinology or orthopedics. And so it's very important that we maintain lines of communication in a multi-directional fashion.

And I think that's all that I have for you today and that's all that Bob has for you. We want to thank you very much and we're eager to take your questions.

Slide 65: Question-and-Answer Session

Anita Welborn:

Thank you so much, Dr. Arceci and Dr. Karp, for a wonderful presentation and this vital information.

It is now time for the interactive part of our program, where we'll take your questions. When presenting your question, please do so general in nature and our speakers will try to respond general in nature as well.

Kristina, can you please give the audience instructions to pose a question to our speakers?

Operator:

Ladies and gentlemen, to participate in the call by asking a question, simply click on Ask a Question, type your question and then hit Submit. Again, to participate in the call by asking a question, please click on Ask a Question, type your question and then Submit.

Anita Welborn:

Thank you, Kristina. We'll take our first question. "Doctors, can you speak to the long-term teratogenic effects of cytotoxic drugs?"

Dr. Robert Arceci:

I'll start with that and as I hope you'll understand, none of us may be complete experts in every aspect of all of your questions, but those of us in pediatrics will often get consulted by obstetricians who call and they'll say, "I have a mother here who's now two months pregnant or six months pregnant and she has leukemia. What can we do and what could the effects be on the child?"

This has been an area that's been completely understudied, but most of us, and I think most people in the field would say, if a woman is less than three months gestation and requires cytotoxic therapy that will cross the placenta, then often an abortion is recommended under those circumstances, although it's always an individual choice. The chances of organogenesis being affected during that critical period of organogenesis is significantly higher.

However, there are in fact reports of some mothers who did not choose to abort, and their children turned out fine.

Now the incidence of birth defects for patients who have been exposed subsequent to the third month have really been almost zero. And so there is a protective effort there by the biology of pregnancy and probably by placental physiology that allows infants to be born without teratogenic effects, although

the drugs are in fact teratogenic, if they were to get across in significant amounts. Radiation to the mother is almost never given any more, but that was at one time an issue. And if a mother has a leukemia, for instance, or a lymphoma, it's almost unheard of that the child will develop that leukemia as well. The only time that this is a risk at all, and this has mostly been reported with very unusual natural killer cell or lymphoid or some myeloid stuff, as well as melanoma, is when a child is in fact immuno-deficient, the baby is immuno-deficient and can't allo-reject that leukemia from the mother. So that's usually never a major concern.

Hope that helps.

Dr. Judith Karp:

I have nothing to add to that incredibly thorough description.

Anita Welborn:

Thank you so much. We also will take our next question. "Can you speak to the research that has been done on chronic fatigue on Hodgkin survivors?"

Dr. Judith Karp:

I'll start out on that. I think truthfully there has been a paucity of research. There has been some. But perhaps not the amount that should be done.

The question about chronic fatigue syndrome, even without Hodgkin disease or other lymphoma, the question what is the etiology is a very important one. And initially it was thought that it was Epstein-Barr virus. And it may still be, although that's not a linear relationship.

About 10 to15 percent of all Hodgkin disease is associated with Epstein-Barr virus, etiologically. Now whether or not that is the subset of patients who develop chronic fatigue syndrome, I don't know. One of the difficulties in studying this is that really in terms of numbers of patients who develop Hodgkin disease per year, it's really very, very small. And so it almost comes down to an anecdote of: this person has Epstein-Barr virus, was this person exposed to some type of pesticide in high dose? I think that my answer to that is there has not been enough investigation, but doing a good investigation is a difficult proposition.

Dr. Robert Arceci:

I would agree entirely with all that Judy just said and just add that chronic fatigue is in fact associated not just with Hodgkin's, but with most cancers. It's phenomenal when you talk to patients about how long these effects can last. I don't pretend to understand I think. But I think it's something to always ask about. Totally understudied.

Anita Welborn:

Thank you, Doctors. Audience for your patients we have available our fact sheet cancer-related fatigue facts. You can speak with the Information Resource Center after our program and they can get that sheet out to you for your patients.

We'll take our next question. "Doctors, is there a specific cancer treatment history and treatment forms with specific follow-up recommendations for that individual that the oncologist can pass on to the patient when cancer therapy ends?"

Dr. Robert Arceci:

This is a fantastic not just question, but idea. And it has not been developed to the extent that it needs to be, but it's something that we certainly have been doing here. The Passport that I mentioned earlier is something that COG, The Children's Oncology Group, will be developing. And what an ideal

world would have, would be that if you have been treated for cancer, you would have exactly that. You would have an exposure history and then a linkage to exactly what you need for follow-up. And when you walked into your private physician's office you could say this is what happened to me and these are some suggestions that have been made to help with that dialogue and that follow-up.

I don't think we're there yet. Even in pediatrics, this Passport to Care, is just being, sort of as we would say, uploaded and worked on. But the CureSeach site I mentioned, that we talked about, Judy and I in the talk, is a great way to start.

Anita Welborn:

Thank you. "Doctors, can you talk about the surveillance and screening that should be done on patients, status post-bone marrow transplant for ALL?"

Dr. Judith Karp:

Yeah, I think this is in many ways, if you can think of it, it could be a complication and you should screen for it. Certainly the screening for immune function is a very important thing to do because of the prolonged need for immunosuppressive therapies, the complications of graft-versus-host, etc.

This may be more common in adults than in children, but there are a number of non-trivial immunologic consequences such as a Sjogren syndrome or a __ syndrome or Raynaud's syndrome, xerostomia, that will last for a lifetime. They're not lethal, but they are chronic and they are problematic and they can lead to other problems as well.

In terms of the transplant itself, there are relapses that occur after bone marrow transplant. And patients should be evaluated for their underlying disorders on an interval basis.

And last but not least, both pulmonary and GI function, liver in particular, need to be monitored. Restrictive pulmonary disease is a very important complication. Malabsorption syndromes are important complications. And another last, but not least, thyroid function and adrenal function. So it's a total body problem, if you will. And so when you screen you should screen for baseline metabolic function and baseline organ function. How often do you do that? The longer the patient lives, the less often you have to do it, but a yearly basis or even when the patient is perfectly well would be what I would think would be reasonable. More in the more proximal time period.

Dr. Robert Arceci:

And I guess I would only add to all of those things the issues of neurocognition. And we see that more in pediatrics I think afterwards. And the other more pediatric-centric view is that if the preparative regimen included total body radiation, those children we now know through work through Steve Sallan's group up north, of us anyway, has shown that there's a much higher incidence of meningioma and malignant gliomas in children at least. And I don't know that for adults. But certainly if a child survivor of a transplant presents with headache and early morning emesis, that's where you look, it's a malignant tumor.

Dr. Judith Karp:

And just one other thing to consider. And that is there used to be this old adage that once you had one malignancy, you're at risk for another malignancy, and then that was touted as an old wives' tale, but I think it turns out that the old wives are right. And that in fact whether this is a unifying defect in the way the individual repairs DNA damage, that's our personal favorite for Bob and me, but there are many other mechanisms we're sure. This is an important issue. And the person may develop a malignancy not even as a consequence of the therapy that they received, they can just develop another malignancy. So that vigilance that you would use, for instance, for all patients over the age of 50 for looking for colorectal cancer, just because your patient had a lymphoma at age 28 or 41 doesn't mean they're not at risk for

colorectal cancer at age 66.

Dr. Robert Arceci:
I couldn't agree more.

Anita Welborn:
Thank you, Doctors. We have another question. "Can you speak to the reoccurrence of non-Hodgkin lymphoma in young adults?"

Dr. Robert Arceci:
And so we cure, and this is an area where it almost is impossible to do clinical trials, randomized clinical trials, because fortunately we have been so successful in treating patients with and children, particularly with non-Hodgkin lymphoma. We're talking, even with stage IV Burkitt lymphoma, 75 percent of children with that disease are cured. The recurrence rates for Burkitt, of course, occurs usually within the first year after stopping therapy, certainly beyond two years usually you won't see relapse in that regard. For other non-Hodgkin lymphomas, in pediatrics, we don't see the indolent lymphomas that are seen in adults like follicular lymphomas. We see very few cutaneous lymphomas. But we tend to see in pediatrics lymphoblastic lymphomas, most of which are T-cell lymphomas. We do see a few anaplastic B- and T- lymphomas. But most of the young children's lymphomas are going to be lymphoblastic and of course Burkitt lymphoma.

So the recurrence rates are relatively low. The therapies have been profoundly effective. We've almost eliminated the use of radiation in most of the treatment of non-Hodgkin lymphoma now, except for central nervous system involvement, for instance, with Burkitt.

I hope that addresses it.

Anita Welborn:
Thank you, Doctor. We have a question from Penny. She says, "When MDS is diagnosed, what is your recommended treatment regimen or is there one, to keep AML and other sequelae and disease development at bay?"

Dr. Judith Karp:
Okay, well, I'm going to be a little bit iconoclastic here. There is this rumor out there that the demethylating agents will prevent the development of AML. If you believe that, I have a bridge for you that I'm selling really cheap. The data, number one, the treatment of MDS as we know it currently, we do not know of anything that will prevent transformation to AML, even bone marrow transplantation. Bone marrow transplantation may be curative for a significant number of people who have bad MDS, but I unfortunately see a number of people who relapsed after transplant for their MDS.

The use of the demethylating agents may extend the time a little bit to the development of AML, but by no means are these drugs curative. We don't know about lenalidomide, but there's no evidence that it's curative. It has a particular role in MDS that's associated with a deletion of a segment of 5q. That's its major claim to fame.

So I'm giving you kind of a negative take on that because I don't think that people should assume that MDS is either easily treatable or curable. It will progress to AML. There are some myelodysplastic syndromes that I fully believe are simply immunologic diseases, that the refractory anemia and sometimes the refractory anemia with ringed sideroblasts. But anything that's got trilineage dysplasia is a stem cell disease that is for all intensive purposes, it's bone marrow failure with excess blasts and that's what leukemia is.

So there you have the negative view.

Dr. Robert Arceci:

And I would agree. We tend to, in pediatrics, not fool around with demethylating agents in the context of MDS, which is quite rare. But we go to transplant as soon as a child develops MDS to the significant level that it is in fact requiring transfusions and all. But once it accelerates, in our world, it's a very difficult disease and in the adult world I would agree with Judy completely.

Dr. Judith Karp:

There's one thing. You can say well, what am I supposed to do, as the physician, what am I supposed to do? Well, what I would say to you is that you have made a diagnosis, you have picked this up and the important thing for you to do is to refer that person to a place where there is an interest and an expertise in hematologic malignancies, in particular one that's doing clinical trials. Because we have a dearth of answers. We've got a plethora of questions, a dearth of answers. And the fact is that if we don't study these diseases and different treatments, we're not going to be any better 20 years from now than we are today and that would be a very sad statement.

Anita Welborn:

We have a question from our audience. This professional wants to know about geriatric survivors of leukemia. He wants to know is there a guideline for surveillance or for screening and if so, for age groups 65 to 75, 76 to 85 and of course over 85 years of age.

Dr. Judith Karp:

It's a wonderful question. It's as key as the key for the younger set. I think that we don't have such guidelines. One place that may approach this is the National Comprehensive Cancer Center Network and I believe that they have just developed a geriatric oncology section of guidelines.

The screening is not going to be any different really than what you should do for a patient who doesn't have a history of malignancy, other than to add on top of that the particular ravages, if you will, of the type of tumor and therapy that the patient may have had. In other words, if you've got somebody who's had prostate cancer and has had a prostatectomy and has problems with incontinence, etc., that's not going to be different just because the patient had prostate cancer. What will be different is that the patient may have had postoperative radioactive seeds placed and that can cause a local radiation cystitis and enteritis.

So I think your question is a perfect question. I can answer it only generically. And it's an area where I think we've not paid much attention until recently because we haven't been able to. But we find now that we can treat patients who are 60 and 65 or 55 or whatever, with very intensive chemotherapy when they have acute leukemia and we can cure some of them, so they're going to live for a while. So we have to be very aware of all of the types of complications that we've talked about today.

I think I would just do age-appropriate screening. Screening somebody at age 85 for just about anything doesn't make a lot of sense to me, but there may be reasons to do that.

Anita Welborn:

Thank you, Dr. Karp, and thank you to our audience for that question. We have a very practical question here. "How do we effectively integrate follow-up between the oncologist, the primary care physician, the cardiologist, all of the folks that are part of the team for the patient?"

Dr. Judith Karp:

I'll try that first. Part of me says that the best way to do that is if you can have your patient followed at an academic center, at a cancer center where all of those specialties are available, you as the primary physician are the front line. You are the ones who will diagnose, you are the ones who will assess

the problems and the amount of damage. And I almost think that in general, for medical problems at least, that referral back through the oncologist is not necessary. I mean, if you sent somebody to me who had a thyroid dysfunction, everybody would be highly displeased. On the other hand, if you let me know, it's entirely possible that I can say I think your friendly endocrinologist is exactly the right person to handle this.

Coordination is a problem. I think it's very difficult in this age of specialization. So I think that if you want to think of this as a tent and the real anchors of the tent are the primary physician and the oncologist, and that between the two of us we can guide the patient. But there is no formula. You have to pick up the phone and make the call. So the communication is no different than it was 25 years ago. And it's no different than if you wanted to refer a patient who didn't have a history of steroid therapy, if you wanted to refer somebody for a hip replacement. You would call your consulting and collegial orthopedist. It would be important in the case of the patient who's had cancer to let the oncologist know as well. Bob?

Dr. Robert Arceci:

I would agree that the coordination is not trivial at all. And I must say that upon referral to a center where you know all of those services exist, it is difficult, and here is truth and consequences, it's difficult here at Hopkins, it's difficult at Harvard, it's difficult no matter where you are in the world to coordinate the schedules of that cardiologist, that orthopedist. And I think at some level we do a pretty good job of that in centers where they provide concierge care. And I must say it's a very interesting observation and let us not get into the politics of whether you're a Socialist or a Republican, but I must say that there are programs within certain hospitals that have concierge care. That is if you come in, you will have your entire day scheduled for you and you will go from the cardiologist, to the orthopedist, to the psychiatrist, to the obstetrician, however you want to go. But that is coordinated through an office.

Now this has not happened for survivors of childhood or adult cancers. And so it's a tremendous amount of effort on the physicians and their non-physician caretaker's part to help coordinate these things. But that is a future that I hope we can achieve some day and maybe create that kind of level of coordination.

But I think Judy is absolutely right. The key is to not to refer somebody necessarily to a cardiologist in this part of the world or that part of the country or that part of the state. To try to find that group that you can work with in a very productive and mutually respectful way and information can flow both ways. I wish it were easier.

Dr. Judith Karp:

But it isn't.

Anita Welborn:

Thank you, Doctors. And we'll take our final question, more than practical and appropriate. "How can we better educate our patients to seek primary care, which in turn can increase their survivorship?"

Dr. Judith Karp:

I will start. Many patients, especially young patients who've had cancer, can have a very devil-may-care attitude. I've looked death in the face once, twice, and I don't really care. I'm just going to go out there and do whatever I want to do.

I think that in part it is the oncologist's responsibility to make sure that patients know that their first line of defense is the primary care physician, who actually has that broad overview and has that ability to coordinate care and to be the keeper of basic good information and do the right studies. So it's the oncologist's responsibility.

It's also the primary care physician's responsibility. We need to refer patients back to you and you

need to keep referring patients to us in a bidirectional fashion for the individual patient.

I think we're in a state of medical expertise and capability, where no one person can do it all, no 25 people can do it all. And so I think that by sharing the patient's care and responsibility, that's probably how we get it done best.

I know that this sounds a little like Pollyanna, but the truth is that we need to keep each other informed and keep the patient at the center of the picture.

Dr. Robert Arceci:

Yes, I think as Hillary Clinton said, it does take a village. And it really does, although she wasn't referring to this, it takes a lot of people to be involved.

Judy's right, we do not do a great job here obviously. And not just here, but in oncology centers, because many patients aren't even followed here, so we're not retaining them throughout their lives. Oncology centers have not been set up in the past to do that at all. We've been very focused on the treatment and the cure, but I think this is changing for the better.

In terms of how you can do this in the office and in general practice, I do think there are plenty of good areas on the web and in the literature. And I would have things in the office, literature, out there. If you or anyone you know is a survivor of childhood cancer, here is some literature that you should be giving your friend, your family member, yourself.

There are multimedia presentations. There are movies out there. The NIH has a program on how to use the media to instruct patients in terms of healthcare. So there are websites on NIH. And I would have that information all around your offices.

You're going to be seeing multiple patients a day who are survivors or who are living with cancer, of course. And I think that making them more aware of this and certainly if we can develop a Passport to Care or whatever we want to call it, this will help as well, so the patients will come to us and to you saying here are my risks.

Anita Welborn:

We thank you all for your thoughtful questions. Our program has now come to an end.

Please join me in thanking our expert speakers Dr. Robert Arceci & Dr. Judith Karp. We are grateful that they have donated their time to us and we thank them for the work that they do in supporting families touched by cancer.

We would also like to again thank Genentech and Biogen idec for their support.

We hope that many of your questions were answered and that the information will assist you and your patients with treatment decisions.

Slide 66: TrialCheck®

The Leukemia & Lymphoma Society is pleased to offer Trial Check to assist patients and providers in locating cancer clinical trials. By answering just a few simple questions a list of available clinical trials related to your cancer will appear in an easy to read list of search results. You may access the Trial Check search tool at www.LLS.org/clinicaltrials or contact the Information Resource Center and a specialist can conduct a personalized search with you.

Slide 67: Co-Pay Assistance Program

We would like to take this opportunity to announce our *Co-Pay Assistance Program*. The program offers financial assistance to qualified patients to help with treatment-related expenses and insurance premiums. Providers and patients may apply online at www.LLS.org/copay or over the phone with a Co-Pay Specialist by calling 1-877-557-2672

Our Information Resource Center is open Monday through Friday, 9am – 6pm ET and specialists are available to speak with you to answer any questions that you may have. The number is 1-800-955-4572.

On behalf of *The Leukemia & Lymphoma Society*, Dr. Arceci and Dr. Karp, thank you for joining us. Our best to you all, good-bye.

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