Corey S. Cutler, MD, MPH, FRCP(C) and Willis H. Navarro, MD
May 20, 2010 ● 1:00pm ET

Operator: Good afternoon, and welcome to Stem Cell Transplantation Dialogue with the Experts, a free telephone webcast education program. It is now my pleasure to introduce your moderator, Ms. Lauren Berger. Thank you. You may now begin.

Lauren Berger: Hello, everyone. On behalf of the Leukemia & Lymphoma Society, thank you for spending this hour and a half with us today, and thank you to Dr. Willis Navarro and Dr. Corey Cutler 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 the National Bone Marrow Donor Foundation for collaborating with us on this program.

You should have received information regarding today's program either in the mail or via email, including an agenda, Dr. Navarro's and Dr. Cutler's biographies and an order form for the Leukemia & Lymphoma Society's materials. We encourage you to look through these materials. You will also find an evaluation form for you to fill out for today's program. For nurses and social workers, you can receive 1.5 hours of continuing education credit. All participants may complete your evaluation form online at www.lls.org/teleconeval. That's T-E-L-E-C-O-N-E-V-A-L. Or, you can use the evaluation form in your packet, and you can mail it in the enclosed self-addressed envelope.

For those of you participating by telephone, you will follow along with the slides in your packet. If you are participating via webcast, you will listen to the program and follow the slides on your computer. If you don't have the slides at this time, you can download them from our website at www.lls.org/survivorship, S-U-R-V-I-V-O-R-S-H-I-P.

After the presentations, we'll take questions from our telephone and our web-based audiences. Today, we have over 2,400 people registered for our program, from across the United States, and several international participants, from Canada, England, Bahrain, Belgium, India, Malaysia, New Zealand and the Philippines. We welcome all of you today.

Lauren Berger: If we're not able to get to your questions, you can call the Leukemia & Lymphoma Society's Information Resource Center toll free at 1-800-955-4572. That number's also on the materials in your packet. We'll connect you with an oncology professional who can answer your questions or order free materials for your needs. Their hours are 9 AM to 6 PM Eastern time, Monday through Friday.

We are also audiotaping and transcribing today's program for posting on the Leukemia & Lymphoma Society's website in several weeks, at: lls.org/survivorship. This provides an opportunity for you to read or listen again to today's program, especially to follow up on the terminology or therapies that you may have missed.

Before I turn the program over to Dr. Navarro, I would like to introduce the Leukemia & Lymphoma Society's President and CEO, John Walter, who will welcome you. John, thank you for joining us.

John Walter: Thank you, Lauren. I would like to add my welcome to all the patients, caregivers, and healthcare professionals on the call today. We are fortunate to have as our presenters Dr. Corey Cutler and Dr. Willis Navarro, both experts in stem cell transplantation, and we appreciate their dedication to supporting the mission of the Leukemia & Lymphoma Society through their work with patients every day. I wish to thank them for taking the time today to provide us with an understanding of stem cell transplantation.

The Leukemia & Lymphoma Society is committed to bringing you the most up-to-date information about your blood cancer. We know it is important for you to stay current so that you can work with your healthcare team to determine the best options for the best outcomes. Our vision is that one day, the great majority of people diagnosed with blood cancer will be cured or they will manage their illness with a good quality of life. Since its founding in 1949, LLS has invested more than $680 million for research specifically targeting blood cancers.

John Walter: We will continue to invest in research for cures, programs, and services to improve the quality of life for patients and families. This program is one step on the road of your journey to managing your quality of life. Thank you, and I'll turn the program back over to Lauren.

Lauren Berger: Thanks, John. I now have the pleasure of introducing Dr. Willis Navarro. Dr. Navarro is the medical director, Transplant Services of the National Marrow Donor Program in Minneapolis, Minnesota. Dr. Navarro's complete biography is included in your packet and I encourage you to read it. Dr. Navarro, thank you so much for being with us, and now I turn the program over to you.

Dr. Navarro: Great. Thanks, Lauren. I really appreciate it. It's a pleasure to be here today, and I want to thank the Leukemia & Lymphoma Society for all that they do for patients and for healthcare providers of patients who have hematologic cancers.

I'll begin now with my first slide. My talk is an overview of hematopoietic stem cell transplantation, and we'll certainly have some time at the end for questions should any issues arise from the slides. I just want to go over my disclosures. As you saw from the title slide, I'm an employee of the National Marrow Donor Program. We're a nonprofit 501C3 corporation.

Here you see a picture of beautiful downtown Minneapolis, which is looking green these days, our Stealth Building, which isn't very well labeled, for the National Marrow Donor Program in Minneapolis, and my home in San Francisco, where I also work and live.

Here's an outline of my discussion today. First of all, I'd like to begin with a description of the types of transplants that are out there. I think there are a lot of terms that are thrown about, and that can be very confusing. My goal in the first few slides is really to explain what the terminology means and what it refers to.

We'll discuss how the matching procedure is done in the case of allogeneic transplants, or transplants originating from someone other than the patient. Last, my charge is to discuss the issues that may come about with quality of life after stem cell transplant.

Dr. Navarro: Let's go over some terminology first. On the first bullet point, you'll see some global terms for marrow transplant. Marrow transplantation can be referred to as hematopoietic cell transplant, hematopoietic stem cell transplant, or bone marrow transplant. Those terms all mean essentially the same thing and are just slightly different ways of saying the same thing. All of those terms refer to the process of replacing the marrow after treatment with chemotherapy, with or without radiation, and now sometimes even with or without immunologic-based therapies, like antibodies.

Other terms that are used are those that identify the stem cell source. The source of the replacement cells for the marrow that's been treated with chemotherapy and/or radiation can be marrow from a donor, from the patient him or herself, or peripheral blood stem cells. Those are cells that are obtained by stimulation of the marrow of either the donor, being the patient him or herself, or a donor other than the patient, typically with a medication called Filgrastim. Then the cells are collected in the same way that platelets can be donated, where the blood passes through a machine that separates out the white blood cell layer that contains the stem cells that we want in order to replace the marrow.

The third source that's becoming increasingly more important is that of umbilical cord blood. These are units that are harvested from generous moms who agree to provide cord blood to a cord blood bank. Those cells that are in the umbilical cord and in the placenta are harvested, then frozen and saved for future use after they've been typed. They can be ordered and shipped relatively rapidly from a variety of cord blood banks around the country and around the world.

The other terminology that's used is to identify the individual who's providing the blood stem cells. Allogeneic transplants are those that use blood stem cells obtained from someone other than the patient. Autologous transplants are those that use blood stem cells that are obtained from the patient him or herself. I want to go over more specific terminology that describes the transplant itself. We talk about the preparative or conditioning regimen. This is the chemotherapy, the radiation, sometimes the antibodies, that are used to help the new marrow to take hold, and oftentimes are also used to try and obliterate or kill any remaining malignant cells.

Dr. Navarro: We also talk about the intensity of the transplant. There's been a lot of interest lately in reduced intensity, or nonmyeloablative, transplants. These are allogeneic transplants where the preparative regimen—the chemotherapy and/or radiation—is geared toward being more immunosuppressive, which allows the new cells to take hold and prevents the recipient's immune system from rejecting those new cells. The goal is there is less to kill (the tumor or cells themselves) and therefore, there's less toxicity of those regimens. It's geared much more toward immunosuppression, which is a key component of allowing an allogeneic transplant to take hold, but has less cell-kill capability, less cytotoxicity, but therefore, less regimen-related toxicity.

Cytotoxicity is a term we use that describes the ability of an anticancer medication to kill cells. The issue with anticancer treatments, that's been the case for many years, is that many of the drugs we use commonly not only affect bad cells—cancer cells—but also affect good cells. That's what leads to some of the toxicities that we see with cancer chemotherapy drugs.

Let me go over some hematologic basics. The blood forming system, or the hematopoietic system, lives in the bone marrow, and that is distributed throughout all the bones in the body, all the way down to the small bones in the ear, and into the pelvis. Everywhere there's bone, there's marrow inside.

Another key element to keep in mind is that the immune system is inextricably linked to the blood system. Any time you replace the blood system, you're therefore also disturbing and replacing the immune system, be it from the recipient him or herself, in an autologous transplant, or the immune system from the donor if the patient's receiving cells other than his or her own.

The other thing to keep in mind is that the blood generating system, the hematopoietic system, is generally the most sensitive organ to the effects of chemotherapy. That's the reason we often see problems with blood counts happening in the course of receiving treatment for cancer in general, and certainly for blood cancers in particular.

Dr. Navarro: What does a stem cell transplant actually achieve? What does it get you? It depends on the type of transplant. I mentioned there are really two basic kinds—autologous transplants and allogeneic transplants. The autologous transplant uses cells from the patient him or herself, and the goal there is to be able to administer very high doses of chemotherapy with or without radiation. The goal of the preparative regimen, which is that high-dose therapy, is to kill cancer cells that may have some intermediate-level resistance to standard chemotherapy doses. The idea is to try and blast away any residual tumor.

The main benefit of an autologous transplant is the cytotoxicity, the ability to kill cancer cells. There is no immune benefit, though, because you're simply reinfusing the same immune system, so there's not thought to be any significant immune benefit of autologous transplant.

For allogeneic transplant, in which we're using the cells that are derived from someone other than the patient as the source of stem cells to replace the marrow, there are two effects: One is the immunologic effect. This is the effect of the donor's immune system coming into the patient and, ideally, recognizing the cancer cells as foreign and attacking them specifically. That can be a very potent and very useful effect that we term (for example, with leukemia) a graft-versus-leukemia effect.

This is what distinguishes an allogeneic transplant from an autologous transplant. It's that immunologic effect—the extra boost you get of not only having the cancer chemotherapy kill the cells that are unwanted, but also the immune effect of the graft coming in, recognizing cancer cells as foreign, and then attacking them.

The flipside of that is, the donor immune cells can also recognize the patient him or herself as foreign and attack the patient cells—the good cells—in which case that is a phenomenon called graft-versus-host disease. We'll talk a little bit more about that in a moment.

Dr. Navarro: The other benefit of an allogeneic transplant is the cytotoxicity effect, the cell kill. But it very much depends on the type of regimen that's chosen. As I mentioned before, sometimes, for allogeneic transplants, a very powerful, very cytotoxic regimen is chosen, where you're trying to still eliminate as much of the cancer cells as possible. Other times the transplant is geared toward using the immune effect that I mentioned as the primary driver of benefit for that transplant. The cytotoxicity may be minimal, and that may be an effort to try and minimize the toxicity from the transplant itself. That can be various—particularly with people who are older, where the high doses of conventional chemotherapy may be just too much for them to bear. That's actually significantly helped with people who are older who still need to benefit from allogeneic transplant.

With the autologous transplant, as I mentioned, the big benefit is from the preparative regimen. It provides a means to give very high doses of chemotherapy to kill cancer cells. In that process, the marrow is damaged but then rescued with cells from the patient. But, as I mentioned, there's no immunologic benefit.

The short-term risks of an autologous transplant are low blood counts, and, often, mouth sores. Because the chemotherapy regimen is very intense and the lining of the mouth—really, the whole GI tract—is the second most rapidly multiplying organ system in the body other than the marrow and tends to be one of the other systems that's particularly affected by high-dose chemotherapy, mouth sores are relatively common.

Patients also sometimes develop skin rashes and organ damage (liver and heart damage). Those things are relatively rare, but that's the reason we check organ function before we embark on an autologous transplant—just to make sure that the main organ systems are functioning properly and able to withstand the intensity of the chemotherapy. Hair loss is very common. Many patients complain of taste changes, because the taste buds are affected by the chemotherapy and the transplant. And a lot of patients complain about feeling "fuzzy." The term "chemo brain" comes about, where patients feel like they're not thinking as clearly. That tends to abate over time. But usually it takes some amount of time, often months, for that to really abate.

Dr. Navarro: From the long-term perspective, patients with autologous transplants face problems with secondary cancers. Unfortunately, the reality of cancer chemotherapy is that, while chemotherapy drugs are important and critical to treat cancer, they do cause DNA damage, which can sometimes lead to second cancers down the road. That's something that has to be weighed in the risk/ benefit assessment of the transplant. But because the frequency of secondary cancers is not very high versus the risk of the ongoing cancer not being treated properly, the vast majority of time, risk/benefit favors proceeding with an autologous transplant when it's indicated. Long-term organ damage, things like cataracts and other issues along those lines, like sterility, are long-term complications that can arise from autologous transplants.

The allogeneic transplant, which is from another person other than the recipient as the donor source, uses the immunologic reaction of the donor's immune system against the cancer cells. It can be extremely potent. The immune effect may be able to kill cells that cancer chemotherapeutics cannot. But the flipside of that is the problem with graft-versus-host disease, where the patient's normal cells are attacked by the new immune system.

Cell kill varies depending on the preparative regimen. We talk about full, or reduced-intensity, or nonmyeloablative transplants, with each of those decreasing in intensity.

The short-term risks of allogeneic transplants depend on the preparative regimen. For those of you who are moving in the direction toward receiving an allogeneic transplant, I would encourage you to definitely discuss the short-term and long-term risks specific to your transplant with your transplant team. That sort of information is contained in the consent form that you'll be asked to sign, that goes over those types of risks. But, generally, the risks for the short-term are infections, until both the immune system and the blood system recover.

Acute graft-versus-host disease, which is characterized sometimes by liver function abnormalities on blood tests, or may manifest as skin rashes, which can range from very mild sunburn-like rashes to very severe rashes, and lower GI tract problems, for example, diarrhea.

Dr. Navarro: Graft failure is also a potential short-term risk where, even though the appropriate number of cells were infused, the graft doesn't take. This is relatively uncommon, but the risk depends on the particular preparative regimen. Unfortunately, no transplant is 100 percent effective for any particular disease, so the risk of relapse for those with malignant disease remains an issue to some degree.

In terms of long-term risks, we are concerned about chronic graft-versus-host disease. Acute graft-versus-host disease occurs typically within 100 days of the transplant. Chronic graft-versus host-disease typically sets in later than 100 days and can be characterized most effectively as very similar to an autoimmune disorder that some people get independent of transplants. Patients may experience problems with their skin getting thicker or tighter, problems with joints and other sorts of autoimmune phenomenon, although in this case, it's really graft-versus-host disease.

Infections remain a risk because it takes some time for the immune system to recuperate and to develop its normal activity against all the various pathogens that are in the environment. Second cancers remain an issue, of course, because of exposure to cancer chemotherapy, organ damage of various sorts, depending on the regimen. Relapse in the long term is still a concern, although less so as time goes by. Sterility is also a concern.

How do we actually go about finding a donor when the transplant that's being proposed is an allogeneic transplant? We at the National Marrow Donor program [NMDP] are heavily involved in this activity. We're searching for donors who have agreed to participate as an unrelated donor for an anonymous recipient. Most transplant centers turn first to siblings as their first-choice donors. But for the people who don't have an appropriate sibling match, then the NMDP is there to help find a donor.

How does HLA work? The HLA molecules are the molecules that are used by the immune system to help distinguish self from things that are non-self. That's obviously very important because, if you have a virus, cells become different from self in some cases,

Dr. Navarro: and various molecules are used by the immune system to detect that. HLA is the system that the immune system uses to make sure that there are no foreign cells invading the body. Of course, with a transplant, that's exactly what we're planning to do. We're having foreign cells come in as the new blood system. But, if we match the donor and the recipient tissue types—and this is not blood type, like A, B, and O, but we're talking about a much more precise, much more complicated system called HLA. If we match the donor and the recipient very well, then there can be, if you will, harmony in the new immune system coming in, in the most ideal cases. The new immune system sets up shop in the recipient, and then develops into, eventually, a normal immune system in the optimal case.

How do we inherit HLA? Everybody has two sets of HLA genes. One set of genes is derived from mom and the other set [is] derived from dad, so, you have two A genes. One A gene came from mom, one A gene from dad—same for B, C, DRB1, and DQ. Each sibling gets one set of genes from mom, one set from dad, and there are two possibilities those sets of genes could be gained from mom or dad.

The long and short is there's about a one-in-four chance that any one particular sibling will be a match for a patient, and that's because—as you see on the graphic—if the patient received the set of genes contained in the A part of dad's genome and received mom's C genes, then you would want to find a sibling who received the same set of genes just randomly. About 70 percent of patients don't have a sibling match, and that's where we turn to the Be The Match Registry to look for a donor who just happened to, by coincidence, have a similar gene profile for HLA.

How do we go about doing the collection? For the donor—be it the patient, a related donor, sibling, or an unrelated donor—a bone marrow harvest is done in the operating room. What happens is the bone marrow needle is introduced into the back of the hip, into the pelvic bone, and repeated aspirations or withdrawals of bone marrow are done, moving the needle around into various spots throughout the pelvis, on both sides and the back.

Dr. Navarro: Typically, we collect, depending on the size of the recipient, anywhere from, say, 300 milliliters—about the size of a can of Coke—all the way up to about one and a half liters, or even two liters if the donor's quite large. And you know how big a two-liter bottle of soda would be—that would be quite a lot.

For the peripheral blood stem cell donation, the stem cell donation is done using the medication Filgrastim, most commonly where the marrow is stimulated for a period of about five days. The donor then goes onto a machine that you see—if you have the slides up, in the bottom picture—the apheresis machine that pulls the blood out from the donor, processes it to remove the white blood cell layer, and then returns the rest of the blood back to the donor.

That process takes about four to six hours and is done over one to two days, depending on what cell dose is required for the recipient. You see, in that third picture, the actual end product. It still looks a little bit like blood because there are some red cells in there, but it's highly enriched for white blood cells and for stem cells that are circulating in the blood because of the Filgrastim.

This is an overview of how transplants actually take place in terms of what the events are. The preparative regimen is given before the actual infusion of stem cells, in order to prepare the recipient, both from an immune perspective if it's an allogeneic transplant and from a cancer chemotherapy perspective in both an allogeneic and an autologous transplant.

We refer to the day of the stem cell infusion as day zero, and the days before that are referred to with minus signs. Following the infusion, we start the count at day plus one, day plus two, etc. We expect that the new blood cells that were infused on day zero will start to grow up in the marrow after they find their way back from the blood, will set up shop in the marrow, and then develop into normal white blood cells somewhere between day plus nine and day plus 28, depending on the type of transplant that was done. Core blood transplants tend to engraft much later, peripheral blood stem-cell transplants tend to engraft fairly early, and bone marrow is in the middle.

Dr. Navarro: What are the issues with quality of life? This is a complicated issue, and it really depends on the type of transplant that was performed. For autologous transplants, it's actually quite a bit simpler for quality of life. It's mainly the short-term effects that affect the recipient's quality of life early on, the things that I mentioned in the prior slides—fatigue, hair loss, taste changes, skin dryness and pigment changes, as well as organ damage. Those short-term side effects certainly can affect quality of life. But most patients recover relatively quickly from those short-term effects, with the exception perhaps of fatigue, where a lot of patients know that it takes several months to start to feel a little more back to themselves—maybe even six months—before really feeling normal again in terms of fatigue.

The longer-term side effects for the autologous transplant are the risk of second cancers and whatever residual effects there may be of any organ damage. But, again, those are typically not big risks, so, autologous transplant really carries the lowest risk of long-term impact on quality of life.

Allogeneic transplant is much, much, more complicated. The reason for that is because we are changing the immune system of the recipient. In doing so, we introduce, potentially, some new issues with graft-versus-host disease.

Some patients will develop no graft-versus-host disease at all in the course of their transplant, while other patients will develop severe graft-versus-host disease that can be an ongoing problem. Some patients will require ongoing therapy for graft-versus-host disease in the long term and will have quality-of-life impairment as a result of the therapy that's required—the immunosuppression—but may also have quality-of-life issues because of the effects of the graft-versus-host disease, in the same way that people have quality-of-life issues that have autoimmune disorders, like rheumatoid arthritis or a disease called scleroderma. These are some of the risks of an allogeneic transplant.

Dr. Navarro: The chemotherapeutic side effects of an allogeneic transplant, again, very much depend on the level of intensity of the transplant. For the most part, though, that's something that would need to be specifically outlined, because it'll vary so much from regimen to regimen in the course of doing the consent process for the transplant.

I think that brings me to the end of my slides. I'll remind everybody, we'll have a question-and-answer session. At this point, I will turn things back over to Lauren to introduce Dr. Cutler.

Lauren Berger: Thank you so much, Dr. Navarro. I now have the pleasure of introducing Dr. Corey Cutler. Dr. Cutler is assistant professor of medicine at Harvard Medical School, Division of Hematological Oncology, in the Department of Medical Oncology at Dana Farber Cancer Institute and Brigham and Women's Hospital in Boston, Massachusetts. Dr. Cutler, thank you so much for being with us today, and I now turn the program over to you.

Dr. Cutler: Thanks very much. First, let me just reiterate what Dr. Navarro said, thanking the Leukemia & Lymphoma Society for all their support, both for patient care as well as the research support that they supply or provide to a number of us at the participating institutions that do stem cell transplants.

My talk for the next few minutes will focus on some of the specific diseases that we perform transplantation for. Following that, we'll go over a couple of the emerging trends in stem cell transplantation research. Once we're done with this portion of the presentation, both Dr. Navarro and I will be available for some questions.

The slide you see here demonstrates graphically some of the more common reasons we perform allogeneic and autologous stem cell transplantation in North America. It takes us a little while to gather data, so this data is a couple of years old, and it is compiled from an organization called the Center for International Blood and Marrow Transplant Research [CIBMTR], a sort of clearinghouse research database for all transplants performed worldwide.

Dr. Cutler:

As you can see on the far left, the disease multiple myeloma is clearly the most common indication for transplantation as reported to the CIBMTR. The majority of transplants for myeloma are autologous.

Going down towards the right, we see a number of other diseases, some of which I'll be talking about. Pardon me for the abbreviations, but they read multiple myeloma, non-Hodgkin's lymphoma, acute myeloid leukemia, Hodgkin's disease, acute lymphoblastic leukemia, myelodysplastic syndrome, chronic myeloid leukemia, and then onto aplastic anemia and others.

Starting with multiple myeloma, we see that, in North America and almost certainly worldwide, this is the most common indication for stem cell transplantation. In multiple myeloma, we almost exclusively perform autologous stem cell transplants.

As Dr. Navarro already mentioned, the purpose of an autologous transplant in multiple myeloma is to try to reduce the amount of multiple myeloma cells that may remain in the bone marrow space after some form of chemotherapy or immunotherapy is delivered. We try to perform this type of transplant whenever the affected patient attains what we call a minimal residual disease state, so that when we collect their bone marrow prior to preservation for the transplant, there is the least amount of myeloma that could potentially be contaminating those stem cells.

Unfortunately, with this type of transplant, there really is no expectation of cure for myeloma. However, we know from several well-controlled and well-designed studies that the use of an autologous stem cell transplant can prolong what we call the disease-free survival, which is the time during which a patient is well without active signs or symptoms of their multiple myeloma.

Because multiple myeloma is a disease that occurs more commonly in the elderly, we do perform autologous stem cell transplants quite routinely for individuals in their eighth decade of life, well into the 70s. Above that, we do hesitate a little bit. But, certainly, individuals up to the age of 75 or so are routinely offered transplant at several centers nationwide.

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Dr. Cutler: The role of transplant in multiple myeloma is evolving quite rapidly, as many new and quite promising therapies have been developed in this disease, which are nontransplant-based therapies, and do question some of the value of transplantation in this disease.

Some other evolving concepts in multiple myeloma include the use of what we call tandem transplantation. Tandem transplantation refers to the sequential delivery of two autologous stem cell transplants performed about three or four months apart. These transplants have to be planned in advance, and all of the stem cells for both transplants must be collected prior to the first stem cell transplant, because our ability to collect stem cells after a transplant is quite limited. This type of transplant is performed mainly for individuals in whom the first transplant does not eradicate the vast majority of the multiple myeloma that we can see on routine bone marrow aspirate and biopsies.

Because each one of these transplants can have side effects or toxicities, the sequential use of two transplants is associated with more side effects. These side effects can be a little more important and can last a little bit longer than after an individual, or single, stem cell transplant.

In multiple myeloma, over the last few years, we've been exploring the use of allogeneic transplantation as well. The difference here is that, because we're using somebody else's stem cells or bone marrow, there is the possibility of an immunologic cure of multiple myeloma. In general, we try to perform this type of transplant shortly after an autologous stem cell transplant, when the patient has the least amount of myeloma in their bone marrow. And because this is a higher risk procedure, it's often performed in younger individuals and more often performed in individuals whose disease characteristics make them high risk for having progressive disease and trouble with their myeloma in the short term rather than the long term. As Dr. Navarro mentioned, this type of transplant, because it's allogeneic, is associated with some degree of risk.

Dr. Cutler:

Moving on to some of the lymphomas, if we look together at non-Hodgkin's lymphoma and Hodgkin's disease, which are two distinct subtypes of lymphoma, these collectively represent the second most common indication for transplant. Again, transplant for the lymphomas is very often an autologous type of transplant.

The reason we do transplant in the lymphomas is to take advantage of the chemosensitivity of the tumor cells. In a sense, when we see patients who have relapsed non-Hodgkin's lymphoma or Hodgkin's disease—for those individuals who respond to chemotherapy—we think that their tumor cells, should any remain after chemotherapy, will be that much more sensitive to very high doses of chemotherapeutic agents. So we deliver very high doses of chemotherapy with autologous stem cells as a rescue to prevent long-term bone marrow toxicity.

We do use allogeneic transplantation in non-Hodgkin's as well as Hodgkin's disease, often for patients who have resistant or multiply relapsed disease. Here as well, it's clear that patients who have disease that is sensitive to the effects of chemotherapy tend to do better with an allogeneic transplant.

We often include chronic lymphocytic leukemia as a subtype of non-Hodgkin's lymphoma, although some of the biology and disease characteristics of this disease are a little bit different. As opposed to routine non-Hodgkin's lymphoma or Hodgkin's disease, we more often perform allogeneic transplantation for chronic lymphocytic leukemia, or CLL. Here, the use of transplant is often assigned based on risk characteristics associated with the disease. It's become more and more common for patients with CLL to have genetic or molecular characterization of their tumor cells, to determine whether they're going to have a favorable or unfavorable disease course with their CLL. We look at things like the genetic changes within the CLL cell, the expression of certain molecules, such as ZAP-70, the rearrangements of the immunoglobulin genes in the CLL cells, to determine who would be a best candidate to have an allogeneic transplant.

Dr. Cutler:

More often than not, we use reduced-intensity conditioning in this type of transplantation, largely because CLL tends to be a disease of older individuals, in whom the high-dose, or big bang, myeloablative conditioning often is contraindicated because of the risk of toxicity and side effects.

Acute myelogenous or myeloid leukemia is far and away the most common indication for allogeneic transplantation in 2010. In our minds, there is a very limited role, if any, for autologous transplantation. It turns out that autologous transplantation in acute leukemia probably is no better than chemotherapy alone.

There are a number of scenarios in which we use transplantation for acute leukemia. For individuals whose leukemia relapses after a first course of traditional chemotherapy, allogeneic transplantation is the only known cure for these individuals. We offer allogeneic transplantation either using high-dose myeloablative or reduced intensity conditioning to all patients who are considered good candidates to undergo transplantation at that time.

However, there certainly are other reasons in which we use transplantation for acute leukemia. More and more, we are realizing the value of transplantation for acute leukemia for patients who are in their first remission. That means patients who have received their first few courses of chemotherapy and who have attained a complete response—no obvious signs of residual leukemia.

When we talk about acute leukemia, we tend to separate patients into one of three risk categories: a very low-risk, an intermediate-risk, and a high-risk category. Individuals in low-risk categories for acute leukemia do very well without transplant. We find it difficult to recommend transplantation for these people routinely, so the vast majority of people who have favorable, or good-risk, leukemia do not undergo transplantation.

The other side of this coin is individuals who have high-risk acute leukemia in whom long-term disease remission and cure is unlikely with chemotherapy alone.

Dr. Cutler:

For people with high-risk acute leukemia, we tend to offer allogeneic transplant in first remission to the vast majority of people, as long as a suitable donor can be found.

The majority of people with acute leukemia, approximately 60 percent, fall into the intermediate-risk category. Here, the role of transplantation has been somewhat controversial. However, it has become more and more of an accepted and probably beneficial therapy for these individuals.

At our center and at some others, we routinely offer allogeneic transplant for patients in first remission with intermediate risk. But, this is very much a decision that needs to be taken in consultation with both leukemia and stem cell transplant doctors, and we do not undertake this decision very lightly.

We use both myeloablative and reduced-intensity conditioning to treat acute myeloid leukemia, depending mainly on patient age, general health, and the comorbidity and toxicity that the patient may have encountered during their prior chemotherapy regimens.

For myelodysplastic syndrome, like acute myeloid leukemia, the only cure we know of is allogeneic transplantation. Here, as well, timing is critical because there are some versions of myelodysplastic syndrome that do very well with supportive care alone, and that means transfusion or growth factors, antibiotics, etc. Because myelodysplasia tends to be a disease of elderly individuals, we tend to use reduced-intensity transplantation more often than not.

Chronic myeloid leukemia, or chronic myelogenous leukemia [CML], used to be the bread and butter for us transplanters. However, the advent of a novel class of agents called the tyrosine kinase inhibitors, including drugs such as imatinib, nilotinib, and disatinib have largely supplanted transplantation. So chronic myeloid leukemia is now, in fact, a very rare indication for transplantation. However, there are individuals in whom the tyrosine kinase inhibitors appear to be ineffective or in whom they cannot be tolerated. Where we find ourselves in situations like that, we do offer transplantation to individuals.

Dr. Cutler:

We sometimes offer transplantation to individuals with CML who are very young and very fit as their first-line of therapy. Individuals under the age of 30 with newly diagnosed CML do extraordinarily well with transplantation, and a consideration can be made to do transplantation early on in their disease course. The alternative is, unfortunately, lifelong therapy with one of these tyrosine kinase inhibitors.

I'm going to move on to some evolving themes in stem cell transplantation research, talking about three topics briefly. First, graft-versus-host disease prevention and treatment, prevention and treatment of relapse, and prevention of complications related to transplantation.

What is graft-versus-host [GVHD] disease? Dr. Navarro has given you a very thorough explanation thus far. As this slide reiterates, it's caused by the interaction between the transplanted immune system or the graft, and the recipient tissues, or the host. For the sake of explanation, I'm going to try to use the situation of kidney transplant to try to explain what GVHD is. If you are a patient in need of a kidney or another transplanted organ, your immune system would recognize that transplanted organ, and you would undergo what is commonly referred to as graft rejection or organ rejection. Note that it's the immune system that does the rejecting of the transplanted organ. Stem cell transplantation is the exact converse of this scenario, because here, the transplanted organ *is* the immune system, and that immune system can go off and attack target tissues, such as the skin, the liver, and the intestinal tract. This is a scenario we call graft-versus-host disease.

We have medications to prevent graft-versus-host disease. In North America, we commonly use a combination of two medications to prevent graft-versus-host disease. We sometimes manipulate the graft itself to take away or to minimize the number of cells that can cause graft-versus-host disease. These are very active areas of research in stem cell transplantation.

Graft-versus-host disease will occur in approximately a third of individuals, up to 50 percent, who have a donor who is a sibling, and will occur in greater than 50 percent of individuals in whom an unrelated donor is used. For cord blood transplantation, because

Dr. Cutler: there are far fewer and perhaps more immature cells in the graft, graft-versus-host disease occurs much less frequently, on the order of 10 to 30 percent or so.

Despite giving medications to prevent it, as I said, we do have GVHD, and we have a number of new and evolving therapies that can be used to treat graft-versus-host disease.

Graft-versus-host disease is caused by the immune system. When we turn down the immune system with GVHD therapy, unfortunately, we end up with a lot of infection. Some of the thrusts in graft-versus-host disease research are to specifically target certain portions of the immune system to turn down graft-versus host-disease but maintain effective immunity, and hopefully, to maintain effective graft-versus-leukemia responses.

As Dr. Navarro mentioned, even though an individual may successfully undergo what appears to be a well-taken transplant, a certain proportion of our patients will unfortunately have a relapse of their original malignancy. This proportion is very highly dependent on the tumor or disease type and the stage at which the patient underwent transplantation, so giving you a blanket number of what is the likelihood of relapse is simply not possible.

But we have ways of trying to prevent relapse or to even treat relapse should it occur after transplantation. The main way we do this is to employ the donor immune system. We either can give a booster of immune cells from the original donor—what we call a donor lymphocyte infusion. We sometimes can try to vaccinate the donor or the donor immune system after transplant to try to enhance an antitumor effect—you give the recipient a vaccine of their own leukemia cells to try to make the donor recognize that leukemia as foreign and fend it off that much stronger. There are now some attempts to augment host immunity after autologous transplant. In autologous transplant, where you don't have the benefit of somebody else's immune system to fight off your cancer, there are ways to try to augment the transplanted immune system to try to make it recognize the original cancer as foreign.

Dr. Cutler: Trying to prevent transplant-related complications also is an active area of research that we're undertaking. Autologous transplant is generally considered a safe procedure, and there's a little bit less research in this field. However, because allogeneic transplantation has a very high complication rate, we are actively looking for ways of preventing or treating complications largely that would affect the liver, the lung, and the kidney. Because these complications have significant impact on quality of life, preventing some of these complications could make transplant that much more tolerable for a larger number of patients, make it that much safer, and increase the accessibility and the acceptance of transplants to the larger patient population afflicted with hematologic malignancies.

At this point, I've reached the end of my slide deck, and I'm going to bring it back to Lauren. I believe we're going to open the floor for questions.

Lauren Berger: Thank you so much, Dr. Cutler. Yes, it is now time for the question-and-answer session. We have many participants on the telephone and on the computer, so please, for everyone to benefit, keep your question general in nature, without too many personal details, so that Dr. Navarro or Dr. Cutler can provide an answer that is general in nature. If you are calling in, your line will be muted after you ask your question, so that one of the doctors can respond. Operator, will you please give instructions to the telephone and web audience so they can queue themselves to ask a question?

Operator: Thank you. To participate in the call by asking a question, please press star, then the number one on your keypad. If you would like to withdraw your question, press the star, then the number two on your keypad. If you are joining us by web, simply click on the "ask a question" button, type in your question and then hit "submit."

We will take questions in the order they are received. Be aware that due to time constraints, we can only take one question per person. Once your initial question has been voiced, I will then transfer you back into the audience line.

Operator: Again, to participate in the call by asking a question, please dial star, one on your keypad, or click on the "ask a question" button, type in your question, and then click "submit."

Lauren Berger: Thanks. We'll take the first question from the telephone audience please.

Operator: Thank you. Our first question comes from Mary Ann from New York. Please proceed with your question. Your mike is now live.

Mary Ann: Yes, thank you very much for your presentations. They're really excellent. I would like to know if you would recommend a transplant for a 69-year-old who has recently been diagnosed with MDS. It is treatment acquired MDS after treatment with FCR [fludarabine, cyclophosphamide, rituximab], because of CLL SLL cancer. It's an abnormal chromosome that's been acquired—321Q26Q. All three bloodlines are affected, very low blood count—I did not respond to last Neulasta or Neupogen any longer—and I am transfusion dependent. I've tried 2 cycles of Vidaza; both of them lowered my blood counts and they do not go up. Would you consider transplant in my case?

Dr. Cutler: Dr. Navarro, I think I'll take that one.

Dr. Navarro: Sure.

Dr. Cutler: What you're describing for the entire audience is a condition we call secondary myelodysplastic disorder, and that's a myelodysplasia that occurs as a result of chemotherapy. Unfortunately, most of our therapies to treat that type of myelodysplasia are not terribly effective, and we often do consider stem cell transplant for secondary myelodysplasia. Whether it's appropriate for you or not is a question that you and your transplant physicians need to discuss. But, yes, in general, we do strongly consider transplantation for individuals with secondary myelodysplasia.

Lauren Berger: Thanks for your question, Mary Ann. We'll now take a question from the web. And the question from the web asks, "If you had an unsuccessful auto transplant and you must do an allo, do you compromise the success and/or effectiveness of the allo if you

Lauren Berger: wait and simply monitor your condition with bone marrow biopsies and PET scans?

Dr. Navarro: I'm happy to take that one. We don't know the disease that this particular question refers to, but in a general sense, a delay in the time from when transplant might be beneficial to the time—if you decide to watch and wait—there could be the potential that the transplant would become less effective over time as the disease progresses, whatever the disease may be. And that would be true for most diseases.

In general, the earlier you proceed with allo transplant, the better the outcome. But, of course, there's the risk and benefit. This is a very complicated decision process, and it really does require that you get input from your transplant center and your transplant physicians, because there's a risk/benefit. If you wait, you have the benefit of having, presumably, good quality or fairly good quality time before you take the risk of going with a transplant, where you could have some quality of life impairment or even die from the transplant versus the risk of decreasing the efficacy of the transplant if you wait over time. There's that time tradeoff of quality time versus the extra benefit of the transplant being done earlier.

Dr. Cutler published a very important paper on this topic, about deciding on timing. I don't know if you want to add anything, Corey, to that.

Dr. Cutler: That paper refers largely to the timing of transplant for myelodysplasia, and it's exactly as Dr. Navarro said. It's a tradeoff. For some types of myelodysplasia, we tend to wait because of the risks associated with transplantation and the relative indolent nature of some forms, whereas for individuals with higher grade or higher risk myelodysplasia, we tend to recommend transplant immediately, because that maximizes overall life expectancy for large groups of patients. Similar types of analyses can be done in other diseases, but MDS was the one we chose for the original type of analysis.

Lauren Berger: Great, thank you. We'll take the next question from the telephone audience please.

Operator: Thank you. Our next question comes from the line of Ellen from Florida. Please proceed with your question. Your mike is now live.

Ellen: Thank you very much for taking my call. I'm a licensed clinical social worker here in Florida, and I'm also calling as a human being who has a friend with non-Hodgkin's lymphoma. She had a few different relapses and was recommended to take autologous stem cell transplant. She opted to fly up to New York to a major medical center because her children live in Connecticut and Manhattan.

When she got there, she was told that the risk for this to be effective was only 30 percent because of the multiple—I think she had two or three—recurrences and that the risk for death was 1 percent. Sadly, she passed away due to an infection, and I did find out after the fact that some hospitals in New York have a policy that people from out of town stay in the area at least till the end of the third month, because that's when infections are likely to happen. She was discharged home to Florida after the second month posttransplant.

I bring this up as an issue for policy as well as for the professionals and the patients, to consider the psychosocial impact of discharge planning. After she died, I looked at the educational file that was left on the web from the website of the hospital. It said that she shouldn't sleep with a cat, she should do certain things for infection.

I bring up a question for your consideration about, number one, is there consistency among the hospitals about time that an out-of-state person is released back home? Also, the PDF file on the website of the hospital said to be discharged to a caregiver. She was a single woman discharged to nobody, staunchly independent, even refused my help at some point. I sensed she had chemo brain. I don't think her judgment was so good.

Ellen: The attending doctor in the hospital admitted that they didn't know how to handle stem cell patients. I'm positive she wouldn't sleep with her cat if she knew this was contraindicated. The question I'm wondering is: For management of these patients, drive the point home about infection risk, because she never told me about being afraid of an infection, or else she would have—.

Lauren Berger: Is the question about policy, consistency of policy?

Ellen: Is there any consistency of policy? I wish the doctor from the New York hospital would call me so I can discuss this with him, but he hasn't returned my call. I think I could help that hospital because I know a lot of details. But the question is—

Lauren Berger: Okay, so the question is about policy, so—

Ellen: And about patient education; either there was a breakdown in discharge—

Lauren Berger: Okay. So we'll try to answer that question.

Dr. Cutler: I think both Dr. Navarro and I will speak to this one, because each individual institution has their own guidelines as to what we do in the posttransplant setting. First, let me also give you my condolences for the loss of your friend. We try to follow our patients closely after transplant. There are certain circumstances in which patients need to return home or out of state. And when that happens, we try to make the best transition to the home environment as we can. Sometimes things are not optimal, but we do what we can.

There certainly are guidelines that have been promulgated from our national organizations on infection prevention procedures after transplant, and we do try to follow them to the best of our abilities. Of course, adults are free-willed individuals and can do what they will.

And I think it's an unfortunate set of circumstances with some communication breakdown. Willis, do you want to comment on this?

Dr. Navarro: I would agree wholeheartedly. We all strive to do the best we can. It's very common that there are not ideal circumstances. We as providers, along with patients, as a team have to make a decision about risk and benefit of a transplant in any kind of setting, be it autologous, as I gather was the case in this one, versus the benefit of the transplant, versus not doing it because of circumstances. I think we all strive to do the best we can. There are guidelines. We have regular transplant meetings annually, and I think that centers adhere to those rules—those guidelines—very well.

I would second my condolences on the loss of your friend. But I would say that, generally, as Dr. Cutler points out, people are free-willed and we have to just deal with that.

The risk of dying is 1 percent, but that means that 1 percent of patients will die of complications. Unfortunately, this happened to be one of them.

Lauren Berger: Thank you for the explanation, and thank you, Ellen; we're so sorry for your loss. We'll take the next question from the web. The person is asking, "Please talk about ALL as an indication for stem cell transplant. How often is transplant used for ALL?"

Dr. Cutler: I could have talked about ALL. It's somewhere towards the middle of that initial curve I showed you in terms of the relative frequency.

Unfortunately, ALL, particularly in adults, is an aggressive disease. It's far less common than acute myeloid leukemia, and as a result, transplant is performed far less commonly overall.

Just like AML or acute myeloid leukemia, individuals with relapsed acute lymphoid leukemia unfortunately cannot be cured with chemotherapy alone. Anyone with a relapse of their acute lymphoblastic leukemia does require a stem cell transplant.

Also analogous to the AML situation, individuals in first remission are increasingly being offered stem cell transplantation as a way to improve their chance of long-term, disease-free cure or survival. We now routinely offer transplantation, using high-dose preparative regimens, to all individuals under the age of 50 with what we call standard-risk ALL. That is the result of a very large

Dr. Cutler: multinational study spearheaded by the Medical Research Council of Great Britain, but also performed in the United States, that suggested that transplant provided superior outcomes to chemotherapy alone for individuals who had a sibling donor with standard-risk acute lymphoblastic leukemia.

Lauren Berger: Thank you. Thanks for the question, and thanks for the answer. We'll take the next question from the phone audience please.

Operator: Thank you. Our next question comes from the line of Claudette from Maine. Please proceed with your question. Your mike is now live.

Claudette: Hello. My husband was diagnosed in 1989 with multiple myeloma and has had two autologous stem cell transplants. The first one lasted about 10 years. The second one lasted about three and a half years. This past year, he went out of remission again in 2009, so had chemo; he had Decadron, Velcade, Aloxi, Cytoxan. He's still in remission, and his protein counts are low, as they need to be. But I wonder, what happens now? There's no more transplants, right, for him? He's 69 years old.

Dr. Navarro: I'm happy to take that one. He actually had a really excellent remission from his first autologous transplant. I would even say that, from the second one, derived a lot of benefit, so those were obviously good things for him to have gone through. At this point, at 69, I think it's very hard for us to say specifically what might be down the road. That's something to definitely bring up with your husband's physician—what the longer term plans might be.

The reason it's very hard to say is because it would depend tremendously on his ongoing medical issues, which we won't have time to address here. But for some patients, even a third auto transplant could be an option, although perhaps not in his case.

The good news about multiple myeloma is that there have been a number of excellent new drugs that have come onto market recently, plus some that are now in clinical trials that are really promising for controlling the disease. If transplant's not an option for him, if he qualifies for a clinical trial—even with some of the agents that are commercially available, as he's on now—those

Dr. Navarro: agents have changed the face of myeloma quite a bit over the past few years.

Lauren Berger: Thanks, Claudette, for your question, and we wish your husband the best. We'll take the next question from the web. The question is, "For an allo transplant, are the immune system benefits of a transplant impacted at all by the degree of chemo/radiation given? That is, if a patient gets a low-dose conditioning regimen, does that have any impact on how effective the immune effect is of a donor's cells?

Dr. Cutler: That's actually an excellent question. The global answer to that, the overview answer, is "probably not," so it's hard to say for sure. If one looks at the long-term outcomes of individuals who have had either a reduced-intensity or a myeloablative transplant for a disease such as leukemia, it turns out that the long-term outcomes are essentially equivalent. However, the causes of failure after the two different types of transplant are a little bit different. The rate of relapse after a high-intensity transplant is a little bit lower, probably on the basis of the antitumor effects of the chemotherapy and not necessarily the antitumor effect of the immune system. However, the rate of toxicity and lethal side effects is a little bit higher after the myeloablative transplant, cancelling out the benefit of the high-dose chemotherapy on relapse rate. So, the comparison for reduced-intensity and fully ablative transplant, is probably the same for patients who are eligible for both.

There doesn't appear to be an enhanced or a reduced effect of the immune system, regardless of the type of chemotherapy that one has had. But there are different effects on the relapse rate, probably from the intensity of the chemotherapy itself. That's my best guess at that, although it's very hard to tease out exactly the immune effects of the donor graft.

Lauren Berger: Thank you. We'll take the next question from the telephone audience please.

Operator: Thank you. Our next question comes from the line of Mary from Wisconsin. Please proceed with your question. Your mike is now live.

Mary: Hi. I'm an oncology nurse in a private practice, and we have a patient who has mantle cell lymphoma. He's very young. He's 33. He's also a Jehovah's Witness. He's gotten two opinions so far, and he's going with our physician. What our physician is doing, is treating him with R-CHOP, alternating with cycles of Ara-C, which I think will be inpatient for a total of six or seven cycles. Then, he's going to proceed with autologous stem cell. I'm just wondering if you have any suggestions on how we can best support him through this. He started with a hemoglobin of 14.5, I believe—very healthy outside of this.

Dr. Cutler: I would refer you to the local Council of Elders of the Jehovah's Witness in your area. They're going to have some material that's going to be able to guide you with what you should be doing. Obviously, you're going to want to focus on strategies that minimize anemia and thrombocytopenia—so very aggressive use of growth factors.

We can't get into real specifics, because there are various interpretations of what a Jehovah's Witness will and will not accept in terms of blood products. That's something that is going to have to be discussed with the Council and the patient. There are publications in the medical literature, as well, that give you an overview of what can be done in this scenario. But this is going to be a tricky scenario for this individual.

Lauren Berger: Thanks for your question, Mary. We'll take the next question from the web, and the question is: "Please talk about donor matches. What is a high point for a match; 12-point match, higher?"

Dr. Navarro: Okay, that sounds like my realm. We look at the different HLA molecules, and we consider one locus, if you will. There's some variability among centers about the degree of mismatch that's acceptable. When you hear the term a 10-out-of-10 match, that means that the donor and the patient are matched at the 2A, the 2B, the 2C, the 2DR and the 2DQ molecules for HLA. That really is the ideal. I don't think too many centers look at 12. They primarily look at 10, maximum. Some centers, based on literature that suggests that DQ is not particularly important, sometimes ignore DQ and only look at eight: A, B, C, and DR, and refer to those matches as eight out of eight when they're ideal.

Dr. Navarro: The level of acceptable mismatch, as I mentioned, varies depending on a number of factors. One is what the transplant center's comfort level is. Some of it's based on the transplant regimen and what they've chosen to use. Some of the reason for the variability is also that some centers have some processing of the graft that allows them to permit more mismatch. Some centers even will do half matches. Those are called haploidentical transplants, where the patient and the donor really only match at—if you were to look at eight—only four out of eight match.

There is quite a bit of variability. What the ideal match is, though, is either 10 out of 10 or eight out of eight. Most centers would do a seven out of eight or a nine out of ten, and then there's a lot of variability after that, depending on the transplant regimens.

Lauren Berger: Thank you for that answer, and we'll take the next question from the telephone audience please.

Operator: Thank you. Our next question comes from the line of Stephen from New Jersey. Please proceed with your question. Your mike is now live.

Stephen: Hello. I have angioimmunoblastic T-cell lymphoma. I've been in remission a little bit over two years. I'm wondering the extent to which a transplant would be recommended to me when and after it returns.

Dr. Cutler: First of all, congratulations on being in remission, and hopefully, you'll never have to deal with us. Should your lymphoma return, it would be one of the types of lymphoma that we would consider amenable to treatment with transplantation after further rounds of chemotherapy, more likely to be in the autologous realm. But the circumstances at that time, should they occur, would dictate the scenario. We hope that you never cross paths with Dr. Navarro and me.

Dr. Navarro: Exactly. I'll second that.

Lauren Berger: Thanks for your question, Stephen. We'll take the next question from the web, and that is, "Why is 60 years of age the cutoff for donating?"

Dr. Navarro: Okay, that's definitely my realm, as well. The National Marrow Donor Program established an upper age limit of 60 primarily based on the fact that once one hits 60 years of age or beyond, the risk for having hematologic cancers, things like myelodysplasia, even AML, increase. That was really set primarily driven by looking at the epidemiologic curves of the incidence of bone marrow problems occurring with increasing incidence as one grows older. This is an area where there's some degree of policy—you could have said 61 or 62 if you look at the curves, or 59 for that matter. But it's an appropriate number based on the increasing incidence after age 60 of hematologic issues, particularly MDS and AML.

Lauren Berger: Thanks. We'll take the next question from the phone audience please.

Operator: Thank you. Our next question comes from the line of Diane from Massachusetts. Please proceed with your question. Your mike is now live.

Diane: Yes, thank you. I was diagnosed with multiple myeloma in 2005, had a transplant in 2006, and have been in remission since. My question is, I am hearing a lot about maintenance after a stem cell transplant now, and do you need to do it right after transplant, or can you still go into maintenance, even though it's been an extended period of time?

Dr. Cutler: The data that supports the use of maintenance therapy after transplant is certainly in evolution, and the larger trials are still being performed. I think this is, again, a question of benefits and risks, probably best addressed with your bone marrow transplant doc. There is likely to be some benefit of maintenance at this point, but you'll have to weigh that against the risks of side effects of medications. I suspect if you've been out of transplant for four years now, you are essentially side-effect free, and you do need to consider the benefits and risks. This is probably a question best addressed personally with you and your transplant physician.

Lauren Berger: Thanks for that question. We'll take the next question from the web audience: "For what reasons, in what cases, would bone marrow harvest be used rather than the peripheral blood stem cell collection?"

Dr. Navarro: I can take that one.

That depends on the setting. For an autologous transplant, the vast majority of centers will do a peripheral blood stem cell collection, primarily because it's actually easier to do, easier to schedule, and so on. Occasionally, in an autologous setting, though, there'll be some difficulty mobilizing—getting the stem cells to actually motivate out of the marrow and into the peripheral blood to do the collection, or the collection will be done and there will be an inadequate number of cells.

There's another new medication on the market, though, that's now made that problem less of an issue, a mobilizing agent. Marrow harvest now for the autologous setting has become very, very, uncommon.

In the setting of an allogeneic transplant using a donor, either a sibling donor or an unrelated donor, the majority of centers who treat adults request peripheral blood stem cells. That's primarily because in adults, the rate of recovery in terms of the blood system is a little bit quicker with peripheral blood stem cells. For the most part, although there's some controversy, most centers feel that outcomes from peripheral blood stem cell transplant, versus bone marrow as the source, are pretty similar.

That is not the case in the pediatric setting. Pediatricians refer to a study that was done through the CIBMTR—that's the International Blood and Marrow Transplant Registry—that looked back at pediatric transplants looking at bone marrow or peripheral blood as the source. There appeared to be, for kids, slightly better outcomes using bone marrow. Once that paper came out, in about 2005, pediatricians have very commonly now, although not 100 percent—depending on circumstance—but very commonly now will request bone marrow rather than peripheral blood stem cells when the transplant is for a child or for an adolescent. That's the primary driver right now for bone marrow collections.

Lauren Berger: Thanks for that question. We'll take the next question from the telephone audience, please.

Operator: Thank you. Our next question comes from Laura from Mississippi. Please proceed with your question. Your mike is now live.

Lauren Berger: Go ahead, Laura. Laura? We'll take the next question from the telephone audience please.

Operator: Thank you. Our next question comes from the line of Lisa from Maryland. Please proceed with your question. Your mike is now live.

Lisa: Thank you so much for taking my question. In the case of high-risk AML that probably developed from MDS in a patient who's over 60, some centers will say in that case they still want to do "the mini transplant," and some will say, no, they would—even over age 60, but under 65, they would do the maxi transplant. Is there any indication which would be better, potentially more curative, in that sort of a setting, in that type of a patient?

Dr. Cutler: As I mentioned before, for individuals who are potentially eligible for both types of transplant, who have AML or myelodysplasia, the outcomes at the end of one or two years are roughly the same, regardless of which of the two types of transplants you undergo. The rate of relapse is probably lower with the high-dose transplant. The rate of side effects and treatment-related deaths are probably lower with the reduced-intensity approach.

Above the age of 60, we at our center tend not to perform the myeloablative transplant unless the patient has very active or resistant disease. I think it's very much dependent on seeing this person in front of you, having a real conversation with them, and deciding what's the most appropriate.

There is certainly no correct answer here. Both are acceptable, but we would tend to favor the reduced-intensity approach in individuals above the age of 60.

Lauren Berger: Thanks so much for that question. We'll take the next question from the web audience: "What are the implications or positives of cord blood stem cell transplantation for NHL, or for any of these diseases?"

Dr. Navarro: I can take that one. Cord blood transplantation has been growing dramatically and now constitutes about 20 percent of the transplants that we facilitate through the Nation Marrow Donor Program.

First, I should say cord blood transplantation, in most centers, is done on a protocol to acquire more data to understand the transplant and its pros and cons more effectively.

Having said that, I think that the benefit of a cord blood transplant really derives from the fact that the requirement for the matching is less stringent, because the immune system of the cord blood unit is much less developed, since it came from a neonate. Because of the less stringent match, the cord blood may be a good source for ethnic minorities for whom there is no adult donor. Cord blood has been an important way for us to be able to meet the needs of folks who don't have unrelated adult donors, and where cord blood may be an option.

The limitation of it is that these units are relatively small in terms of numbers of cells. Oftentimes, in order to do the transplant in an adult, with the cord blood unit, you actually may need two units. That has been an ongoing area of investigation and looks very promising as a methodology to overcome the fact that the units are relatively small for a normal size adult.

Cord blood is actually very interesting and an important area of transplant research right now.

Lauren Berger: Thank you so much. And thank you so much to all of you for all of your questions. Our program has now come to an end.

Please help me thank Dr. Navarro and Dr. Cutler. We are so grateful that they have donated their time today, and we thank them again for all the work that they do every day in supporting families and individuals touched by cancer.

We hope that many of your questions were answered, and that the information will assist you and your families in your next steps.

Lauren Berger: Our Information Resource Center is open, and our specialists are available to support you and to answer any additional questions that you may have.

Please complete an evaluation. We really appreciate your feedback to help us plan future programs.

As a reminder, you can submit your form online at: www.lls.org/teleconeval, T-E-L-E-C-O-N-E-V-A-L. That is on the materials in your packet, or, you can enclose it in the envelope provided and mail it back to us.

On behalf of the Leukemia & Lymphoma Society and Drs. Navarro and Cutler, thank you so much for sharing your time with us today. Good-bye, and we wish you well.

Operator: Ladies and gentlemen, this does conclude today's conference. You may disconnect your lines at this time, and we thank you all for your participation. Have a wonderful day.