Carrie Callas: Good afternoon, or morning, for some of you on other time zones. Thank you for joining us for Transplants 101, Introduction to Bone Marrow and Stem Cell Transplants. My name is Carrie Callas. I'm the Director of Programs at the Leukemia Research Foundation. This program today is being offered in partnership with the Blood and Marrow Transplant Information Network, BMT Infonet. The Leukemia Research Foundation's mission is to cure leukemia by funding [00:00:30] innovative research and to support patients and families. The foundation has raised over $83 million in support of its mission and has funded research grants to over 600 new investigators worldwide. Our free support programs for leukemia patients and their loved ones include information and resources, education programs, peer support services, financial assistance, and a directory of other helpful organizations and resources. Coming up in February [00:01:00] and March, we're hosting two leukemia Q and A programs, which is all question and answer session of a panel of experts, which you'll receive more information on through email or you can register on our website leukemiarf.org.

[Instructions for participants omitted].

I would like to now introduce our program partner Marla O'Keefe, who is the director of outreach at BMT Infonet.

Marla O'Keefe: Thank you Carrie. My name is Marla O'Keefe and I am the director of outreach at BMT Infonet. Thank you again to Carrie and the Leukemia Research Foundation for including BMT [00:02:30] Infonet as a partner in this important and informative webinar. For those not familiar with BMT Infonet, we are a nationally recognized nonprofit that provides transplant recipients and their loved ones with emotional support and high quality, easy to understand information before, during, and after transplant. Our goal is to empower patients with credible information so they can take a more active role in decisions affecting their health and treatment options. [00:03:00] It is now my pleasure to introduce today's speaker, Dr. Tulio Rodriguez. Dr. Rodriguez is a hematologist oncologist specializing in bone marrow transplants and asthma healthcare. He has performed over 2,500 bone marrow transplants throughout his career. He has also published work, and lectured widely, on a range of medical topics. Dr. Rodriguez has devoted much of his research career to the study of hematopoietic stem cell transplantation [00:03:30] and hematologic malignancies. Take it away, Dr. Rodriguez.

Dr. Tulio Rodri...: Thank you so much. So thank you for [00:04:00] the opportunity of offering this introduction to stem cell or bone marrow transplantation today. I'm sure you all know it's a technique that provides an opportunity of a good outcome when sometimes other treatment options don't work as well, or take patients who have a high risk of not responding well to standard therapy and bring the hope [00:04:30] of a successful outcome. So the idea this afternoon is to provide some basic information, and hopefully we're going to set up a platform for discussions of your questions in special circumstances. Now, that being said, I

want to make sure that we understand that what we discuss today is very in general and not necessarily applies to your specific [00:05:00] situation or condition, and should not replace your conversation with your physician or provider. Now, let's move forward.

Yeah, so everything starts with tumor growth. Doesn't matter what type of malignancy we are talking about. Tumor growth occurred [00:05:30] either if it's leukemia, breast cancer, colon cancer, you're going to have a cell that becomes a malignant cell and start growing excessively in the body. As you can see in this cell culture by the second row on the first tile, that arrow A is pointed to the first sign of our cell division. If you follow to the left you can see how there's like [00:06:00] an appendix that is coming out of from that cell.

So chemotherapy, what it does is that is going to stop the reproduction of these cancer cells, and they prevent this cell from growing and spreading in the body. Everything starts with a cell [00:06:30] that becomes a tumor, so now chemotherapy is going to debug, or eliminate, most of these cells. And that's kind of the problem that many times after standard chemotherapy you kind of leave behind some cells that can lead to the regrowth, or tumor recurrence expansion, of that tumor growth.

So the question here is, if that's the case, why we [00:07:00] don't use a more potent medication, why we don't use a chemotherapy drug that can get rid of every cell? Well what happens is that in the same way that there's a growth of tumor cells, there's some normal cells but they're sharing this characteristic. For example, in our blood cells, we all know that red cells, they have the function of carrying oxygen throughout our bodies, but they last in [00:07:30] our bodies only 120 days. Right after 120 days our bodies used the red cells and they need to be replaced. Actually platelets, some of you might know, the cell, they work like the plumber's seal. They last only approximately seven days. And the white blood cells, which are supposed to protect us from infections, they last four to six hours. So our bone marrow, through a process that is [00:08:00] known as hematopoiesis, is responsible for the formation of all these blood cells from the hematopoietic stem cell that can be found in the bone marrow.

So if we try to eliminate all these malignant cells, unfortunately we're going to deplete our bodies of necessary cells that we need in order to survive. So as a technique to overcome this challenge, we have what we call stem cell bone marrow or [00:08:30] stem cell transplantation. In this cartoon, the green side, the bottom part, is depicting a description of allogeneic stem cell or bone marrow transplant. In this case you have the patient who is exposed now to a higher dose of chemotherapy, sometimes radiation therapy, and simultaneously you have a donor that has been tested in a HLA match [00:09:00] and is serving now as an allogeneic stem cell donor. So through this stem cell collection or donation, now this patient can receive a transplant after having the treatment eliminating those cells that we were referring to prior. So a variant of this

technique that sometimes is been used, for example for other hematopoietic malignancies like [00:09:30] lymphomas, multiple myeloma, the patient once has received therapy and the disease is eliminated from the bone marrow, now this individual can serve as his own donor.

So the collection of stem cells take place, in this case, because the patient now needs to go through the conditioning regimen those cells needs to be put in a freezer right at very low temperatures in order to protect them from the higher doses [00:10:00] of chemotherapy. But after the conditioning regimen, basically the same thing happens with all the cells and they are transplanted. So these are the two main type of stem cell or bone marrow transplantation. But for patients with leukemia, more often what they go through is through an allogeneic transplant.

So the bone marrow stem cell collection can be obtained in [00:10:30] two main ways. One is the bone marrow harvesting where the donor goes into the operating room and is put under general anesthesia. This is a patient in the prone position on his belly, and simultaneously the surgeon and the assistant are going to extract bone marrow directly from the iliac bone. So in this case, the procedure is performed sometimes in [00:11:00] less than an hour. However, a patient need to be exposed to general anesthesia.

On the other hand, the peripheral stem cell, which is what you have on your right, it works by mobilizing the stem cells that you can find inside the bones into the peripheral blood. Once the stem cells are in the peripheral blood, they're going to be filtered through a machine that has like a centrifuge inside, and by density we can select [00:11:30] the stem cells and the rest of the blood comes back into the body of the donor. And remember that in this part, the patient who is going through an autologous transplant or a stem cell donor who is serving as a stem cell for an allogeneic transplantation, they both can go through both type of techniques. Although both of them they have a pros and cons and some of them have been associated with better outcomes, faster [00:12:00] engraftment, some others are better alternative for certain diseases. So that's why it's so important to this cause with your bone marrow transplant provider, what is best for your specific case.

Now what about transplant per se? Well, the technique has become more popular because it's more effective and safer. The truth is that the first time that a stem cell transplant patient [00:12:30] took place, the way that we know stem cell transplant today, was in the late '50s, early '60s. And I want to remind everybody that back then, not only the technique was in their first steps, but also the supportive care was not as good as what we have today. We didn't have the same antibiotics that we do have today. We didn't have some of the antivirals or antibiotics against viral infections. [00:13:00] We didn't have these antibiotics against fungal infections. We did not know how to match donors so effectively as we do know today.

So the treatment became less problematic, there were less challenges, there was more effectiveness, and something that was done only for patient with poor prognosis, a patient who did not have any other options. Today, allogeneic transplantation [00:13:30] and even autologous transplant is being done for patients who are in better shape, patients who we believe they have a high chance of a relapse, a high chance of having the cancer back. So we no longer wait until patients are sick or they don't have too many options to perform this. So the orange line, for those who are not familiar with this graphic, remember that the horizontal line, what are known as the X axis, give us [00:14:00] the year, right? So from 1970 to 2016, and then the number of patients is on the vertical line, or Y axis. So the way that this work, when you have 50,000 patients, you throw a line that goes horizontally and then when it interlocks with the vertical line, or intersect, [00:14:30] is when you throw a point. And the same thing continues over time depending on the number of patients and then you throw the line.

That's how we know that over several years the number of autologous transplant have been going up significantly. The same thing is happening with patients who undergo a related donor transplants and those who are recipients of unrelated, which [00:15:00] basically is kind of a more novel therapy has been evolving and more numbers are being present nowadays.

Now the transplant, as I mentioned before, they have several indications. Here we have data from the Center for the International Bone Marrow Transplant Registry, or Research. And this is by disease. Again on the X axis or the lower line, we have [00:15:30] the different type of malignancies, lymphomas, plasma cell disorders, or multiple myeloma, amyloidosis. We have AML, other malignant diseases, ALL, CML, et cetera. We have the MDS and the myeloproliferative neoplasms or diseases and the CMML falls in this category, plastic anemia.

Now the color tells you the type of transplant that more often these patients are going to receive. So the orange represent [00:16:00] autologous transplant. So the way to read this bar is that the patients with lymphoma more often receive an autologous transplant. Some of them are going to be recipients of allogeneic. I can tell you that most of the time that happens when the autologous transplant doesn't work. On the other hand, patients with AML very rarely receive an autologous stem cell transplant. Most of the time they will be recipients of [00:16:30] allogeneic transplant. And that makes sense in the case of AML, that disease is a disease of the stem cell per se. So using an autologous stem cell graft might not be the most effective way to do this type of transplant. So again, the two type of indications or diseases that receive a total transplant more often [00:17:00] are non-Hodgkin's lymphoma and plasma cell disorders, multiple myeloma, amyloidosis. On the other hand, leukemia, for the most part they're going to be treated with allogeneic transplantation, either AML, ALL, CML, et cetera.

Now when we try to take someone into transplantation, when someone comes for evaluation, there are three factors that we take in consideration. Of course we have in front of us a patient, so [00:17:30] we don't treat myeloma, we treat a patient with myeloma, we treat a patient with AML. So I believe that this is one of the most important factors in the process of making a decision about if someone needs a transplant or not. The disease is important as well, because some diseases can present with high risk characteristics that tells me if the disease is going to be resistant [00:18:00] to therapy most likely, or there's going to be a chance of recurrence. And last but not least, the source of those stem cells that are going to be used in the transplant. Are we talking about a donor that is a sibling, a full match, or are we talking about an unrelated stem cell donor that as much as the technology tells me that they are identical, they are not really related by blood so there's some minor antigens that are absolutely they're not going to be [00:18:30] matched.

And we also have performed some transplants using stem cell from umbilical cord blood. And usually this is done for patients who really needs a transplant but unfortunately don't have a suitable donor among siblings or in the registry for unrelated transplant. Remind ourselves that among the siblings only one out of three patients who need a transplant are [00:19:00] going to find a donor among their relative. So these are the three important factors. And for example, if you have a patient who is in good shape, young, strong, no diseases, no comorbidities. And on the other hand you have a disease that is very aggressive and you have a donor that is a full match and it's a sibling. I mean that is a straightforward, we have the triangle that makes me think yes, this patient absolutely needs that transplant.

On the [00:19:30] other hand, if I have a patient that is very frail, is very sick and you have a disease that has a low chance of recurrence, and I have no donor, I have to look for a non-related or a cord blood stem cell transplant. I think that will need really special circumstances for someone serious to offer a stem transplant to that individual. So this kind of mind process help us to identify and select who [00:20:00] will benefit for stem cell transplantation.

Now some risk factor for this transplantation, I mentioned the patient disease and bone marrow world. So age. Age has been seen that correlates with outcomes. The older the patient, the higher the chances of having more complications. And in some diseases that have been found even to be 36, 39 years old, like in the case of chronic myelomonocytic leukemia. In some others, 60 [00:20:30] years old.

Now I have always remind residents, fellows, people who are in training that risk factors like side effects from any drug is not there to refrain yourself from offering a treatment. Patients need a therapy. Those are there for us to identify those risk factors and to get prepared to come up with a way or solutions to mitigate the risk. To know [00:21:00] that the risks are there so you get

prepared, not to tell someone, I'm sorry, go home because your age is prohibitive. Because there's not such a thing as we'll see shortly. Comorbidities is very important. Obviously comorbidities that are not well controlled. So someone who comes with high blood pressure but is on medications and the high blood pressure is very well controlled, there's no reason whatsoever not to offer life-saving stem cell transplant to that individual.

Something that sometimes we forget, social determinants [00:21:30] of health, what are those? Those are conditions that are not necessarily physiologic, right? But they have a very important weight on the outcomes of this patient. Do they have transportation? Are they depressed? Do they have this caregiver? So those aspects that not necessarily has anything to do with health but they're extremely important at the time of the outcome of transplant needs to be evaluated, and most [00:22:00] transplant programs of quality are going to have a designated social worker who's going to be looking into this. They're going to have a navigator or coordinator who's going to be helping with this social determinants of health. As I mentioned this is, it is a high risk. Someone who's in remission, the outcome might be different, compared to someone who you do a transplant in relapse or in refractory disease, or the disease is circulating to the bloodstream and relapse [00:22:30] disease. They don't have the same outcomes of patients who go into transplantation at the first time of their complete remission.

I mentioned the source, autologous. I mentioned the age of the patient. What about the age of the donor? That is a debate. In some diseases this has been found to be a factor, like in DML for example. In some others that has not been found to be important. And the other variant here is that when it's a sibling, the donor age [00:23:00] is, doesn't seem to be as relevant as when we're talking about unrelated stem cell transplantation. Now the human leukocyte antigen match donor is important. Allogeneic related, unrelated, allogeneic related mismatch, or we call this haploidentical transplant, and umbilical cord.

Now graft versus whole disease is a potential complication of allogeneic transplantation, can be acute [00:23:30] usually within 100 days, or chronic after 100 days. Can be some organ damaged liver toxicity, this is what we call being occlusive disease. Infections. Infertility is often important to discuss with young patients that, so there's some ways of trying to maintain fertility or to do some sperm banking, cell banking, et cetera.

Secondary malignancies is something we need to be in mind. Alopecia [00:24:00] is almost universal. And something that we want to maintain in our mind is that graft versus host disease is not always detrimental, right? So not everybody's going to have graft versus host disease can be very mild, however, in some cases can be severe. A chronic graft versus host disease usually shows up on patients who had an acute graft versus host disease, but interestingly with this graft versus host, [00:24:30] which is that the cells from the donor that

are inflaming the body of the patient, the recipients, but this kind of inflammation, quote unquote inflammation, comes with a graft versus tumor effect. So what we have seen is that patients with chronic graft versus host disease can get cured from their diseases more often than when you don't have graft versus host disease. Again, doesn't mean that it's zero, and patients who have never seen GVHD absolutely can get cured from their diseases. But [00:25:00] chronic graft versus host disease can bring an additional immunologic attack to the malignancy.

Now this is a graphic from the CIBMTR, or the Center for the International Blood and Marrow Transplant Research. These are the number of years from 2000 to 2020. Looked at peripheral blood stem cells is what have been done more often during those years. The blue part of the column means patient who received [00:25:30] bone marrow. So absolutely when we're talking about match related donors, more often they receive peripheral blood stem cell transplant. In the case of hypo identical the same thing, but look how the number of hypo identical transplant continue to increase over time and they're significantly in higher numbers in 2019 and '20 compared to a thousand. And again more peripheral blood than bone marrow.

Also the same thing happened with cord [00:26:00] blood. There was kind of a boom in the cord blood. Remember that cord blood is a very small amount, so most of the time was done for children. We have done cord blood for adult as well. But this is kind of a lacking popularity. It is kind of a difficult immune reconstitution. How the cells function over time is difficult. I have seen patients with significant infections even a year later after their cord blood transplantation. And what happened is that the hypo identical [00:26:30] transplants continue going up as you can see here, especially in patients older than 18 years old.

Now this is kind of an important slide and we're almost done with this part of the presentation because I think that the most important part is the question and answer, but I think that it's important to demonstrate that from 2005 to 2020, the number of patients who are older than 65 years old receiving allogeneic transplant has increased significantly. [00:27:00] This is expressing percentages. So in 2005, only 4% of the patients are recipients of allogeneic transplantation for malignant diseases were older than 65 in comparison to 27% of the patients now receiving stem cell transplantation, they're older than 65 years old.

And this includes patients with AML, ALL, MDS, or MPN, and lymphoma. Now [00:27:30] as I mentioned from the beginning, the technique has improved and this is an Alliance trial that Alliance made that several group of researches got together, put their efforts together. And again in the horizontal line, or X axis, you see number of months, 12 months or a year, two years, three years up to five years. The red line is the allo transplant, the blue line is the standard

[00:28:00] chemotherapy. And for patients, of course, in good shape, selected patients from 60 to 75 years old, transplant patient does better than standard chemotherapy.

So for us to tell someone that it's because that person is older than 60 years old should not get stem cell transplantation, we don't know what we're talking about when we say that. Stem cell transplantation absolutely can offer a chance of a better outcome, again, for selected individuals [00:28:30] in good shape, and this is, again, transplantation. If we look into multiple myeloma, these are autologous transplant. We saw if we take patients who are older, 70 years old or older, and the segmented line is patients who are younger than 70 years old. In this case, both of them goes into transplantation. You see the probability of continuing with a progression-free revival is identical. Doesn't matter [00:29:00] if you're older than 70 or you're younger than 70. The same thing applies to survival. At 10 years the overall survival is almost identical between both groups. So for us, I can tell you that we have transplanted patients. The oldest patient that I remember in this institution, 83 year old and he's still alive doing well. And he came with refractory lymphoma, it was like three years ago and he's traveling, he's perfectly fine.

[00:29:30] So in conclusion, bone marrow stem cell transplantation allowed for the delivery of high doses of chemotherapy and/or radiation therapy by replacing or rescuing the bone marrow that is being damaged by the necessary treatment. Now the number autologous, allogeneic related, allogeneic unrelated transplant patients in the United States has increased since 2000. The number of allogeneic transplant for the treatment of malignant diseases in patients who are older than 65 years old continues to increase. And in 2020, [00:30:00] for example, 27% of allogeneic transplant recipients were older than 65 years old as we saw. The use of reduced intensity chemotherapy or conditioning regimen or normal mobility therapy, we didn't talk too much about that. But for that it's a less intensive chemotherapy, and of course patients should be in remission. It's difficult to do a reduced intensity if you have active disease.

But this was using 60% of all the patient recipients of hyper identical transplant in [00:30:30] 2020. And allogeneic bone marrow transplant stem cell transplant patient has a potential of reducing relapse rate and superior long-term survival relative to chemotherapy in selected older patient with ML, especially those who are in their first complete permission.

And with this I would like to stop in order to open the forum for our speaker and after that I'll be happy to try to answer some of those questions. Thank you for the attention and I hope you take as much as you can from this information.

Carrie Callas: [00:31:00] Great, thank you so much Dr. Rodriguez for that very helpful overview about transplants. And Dr. Rodriguez will be right back with the Q and

A session. But before that I'm going to go ahead and introduce Bob Trevor, who is a patient who has undergone a transplant and he wanted to share some of his experiences and kind of what to expect with our participants today. And then immediately [00:31:30] following, we will spend a little bit of time on the A and A. So Bob, I would invite you to go ahead and get started.

Bob Trevor: Okay.

Carrie Callas: Thank you.

Bob Trevor: Okay. Yeah, thank you. Thank you Carrie. Yeah, and last week actually represents my 10th anniversary of the transplant, for which I'm very grateful. So in 2012, six months before the transplant, I was diagnosed with aggressive AML [00:32:00] with a flipped three mutation for fast relapse as the cherry on the top. So I started my induction and consolidation with the chemo Idarubicin, which I remember because it sounds like a woman's name. Idarubicin, Maisie Rubicin, whatever. And I did well, I did not have any kind of side effect, no nausea. I mean I had tubes coming out of my arms, I had blood transfusions, I had platelet transfusions. But I was pretty [00:32:30] good, and I was jolly. And in fact, I even made up a little song which entertained the nurses. Leukemia, leukemia, leukemia. You're taking my blood cell and run Venezuela. Everybody. And it turns out one of my oncologists was Venezuelan. So they really appreciated that.

So I go through all that kind of skipping through life and feeling fairly good. Then we find a donor, an unrelated donor, [00:33:00] to give me cells, stem cells. And I asked, look, can I wait a little bit? It's coming up to the Jewish holidays. I'd like some spiritual fortification before I get this transplant, because I know there will be probable GVHD and other things to deal with. He said, you're doing so well. Everybody agreed, go ahead, go to services, get your spiritual fortification. I did. And two days after Yom Kippur, I relapsed.

[00:33:30] City of Hope has like a minus four, minus three, minus two. At minus two they said, we have to stop this. You've relapsed. We can't give you the transplant and we don't know how to get you back into remission. And I said, well I guess I'm not being written into the Book of Life this year, eh? The important thing, part of this is you've got to keep a sense of humor about everything as much as you can. I remembered a colleague who 20 years before had leukemia. [00:34:00] I contacted him, he suggested I get to the Hutch in Seattle, Seattle Cancer Care. They had the most cutting edge leukemia treatments. The great late Elihu Estee suggested I get the G-CLAM treatment, which is also known as the Polish Protocol. This is verbatim, I'm not making this up.

G-CLAM is an acronym for five different very strong chemos. And the Polish part is they found 50,000 milligrams [00:34:30] of statin has a way of socking the

chemo in to fast relapse patients. So I went back to Seattle, Kaiser agreed to administer this chemo, and it worked. It kept me alive except the original donor was no longer available. So they had to find a new donor, and in the meantime they removed my immune system. So anybody visiting, my very gracious and generous wife visited me almost [00:35:00] every day. She had to wear a hazmat suit. I could not get any kind of infection, or again, it would be no transplant and my chances of survival would be minimal. So it took another, I don't know, two and a half months to find someone. And it was unrelated, as I said, thank God for her. She was a young woman, ironically from my hometown in Philadelphia, as I later found out.

So I got the transplant, [00:35:30] the stem cells, and then it wasn't so much singing and dancing. It was tough. It was a tough road, but I'm very grateful to have gone through it. There'd be a bunch of us, apparently the City of Hope, once you get the transplant, you have what we call the pagoda. It's like several layers of bags and stuff. Have I reached my five minute yet? And it was tough, but my tips [00:36:00] that I can give you, to those looking forward to it. If you're offered the transplant, get it. Keep your sense of humor whenever possible. Try to have somebody special in your life, a spouse, a good friend, to help you see through it, see it through with you. And one more tip, slightly off topic, but I think legitimate, there's a movie out called Living, which is, I think critical for any person facing a mortal disease to see. Part of the message of this [00:36:30] film, beautiful film, very quiet, nuanced, is do some good in this world while you can. And so I guess that's close to my five minutes. So there we are.

Carrie Callas: Thank you so much, Bob. It was so kind of you to share your experience and to give your tips and hope for those on the call who are about to go through this or their loved one is. So thank you so much Bob. I greatly appreciate you being here. [00:37:00] So now I will ask Dr. Rodriguez to come back on, and Marla from BMT Infonet is going to help facilitate the Q and A session.

Marla O'Keefe: Okay, great. Thank you. Bob, thank you for your story. And Dr. Rodriguez, thank you for the excellent presentation. We have a number of questions, so I kind of organized them a little bit. There are a number of questions on age. Someone asked if people over 80 years [00:37:30] old can be transplanted, and if there is an optimal age for transplant.

Dr. Tulio Rodri...: So most patients who are older than 80 years old are going to be recipient of autologous transplantation. Allogeneic transplants at that age sometimes can become challenging, but as I said before, this should not replace a conversation with your physician. There's some case reports [00:38:00] of our patients who have gone through allogeneic transplant at 80 and beyond. So it's not that it's unheard. That being said, it's not the most common type of transplant at this point in time.

Marla O'Keefe: Okay, thank you. How can family members test to see if they're a match?

Dr. Tulio Rodri...: Well, they can certainly go to their, actually [00:38:30] we do that through our center, the National Marrow Donor Program has some events and you can call them directly and they can direct you to the organization in your state. Here, for example, in Illinois Life Source was one of the organizations that was kind of doing that. But in your center sometimes they can collect the samples and sometimes even with a mucosal brush is all what it takes.

Marla O'Keefe: [00:39:00] And if a family member does match, what is a procedure for, how do they go about donating?

Dr. Tulio Rodri...: That is an excellent question, because something that usually happens once the sibling or family member is identified, they go through a workup to make sure that that patient is in good shape to donate. Because many times is known [00:39:30] that the donor and everybody is kind of sensitive and anxious about not receiving something or any transmission of infectious diseases. And of course we all look for that. But something that we want to make sure that everybody out there understands is that the donor becomes our patient, and actually we use a different transplant physician for level eight donors, or a different provider, it can be a bone marrow transplant nurse practitioner, to make sure that there's no [00:40:00] conflict of interest. That individual is going to be making sure that the health of that donor is the priority for that provider that is evaluating that donor. So the donor is going to, we're going to be taking care of him or her to make sure that both individuals and healthy.

Marla O'Keefe: Great. How is it determined whether a patient will be [00:40:30] using their stem cells or a donor's?

Dr. Tulio Rodri...: So most of the time is it because of indications. Leukemias, for the most part, they're going to receive donor stem cell transplant. In very rare cases, a patient with AML in a low risk, in some research they have used autologous stem cell transplant, but that's not the norm. The norm is that autologous are reserved for lymphomas and multiple myeloma, while leukemias, [00:41:00] they received donor stem cells.

Marla O'Keefe: Very good, thank you. Is there any way, this is kind of a hard question. How is the success of a transplant calculated? We get those questions a lot at BMT Infonet. I mean is there any straightforward answer to that?

Dr. Tulio Rodri...: Yeah, yeah, because what the patient and I care about is survival, right? There's many surrogates in institutions use engraftment on how many [00:41:30] days the cells are coming up and the patient can leave the hospital. That is a success transplant in the eyes of a certain individuals. But at the end of the day, I want to make sure that the patient who comes here, or comes to any center with a disease, has AML as Bob mentioned, when I check on him a year later, he's still

around functional doing well. That in my eyes is successful stem cell transplantation. That's how you measure them. Again, yes, you can measure successful [00:42:00] transplants about how quickly they left the hospital, if they develop infections or not, how many transfusions they received, et cetera.

Marla O'Keefe: Kind of tagging along with one of your answers that you just gave, how long do patients normally stay in the hospital post-transplant? Is it a set time or does it vary?

Dr. Tulio Rodri...: Yeah, I mean each individual is a little bit different [00:42:30] because I mean some patients might develop some complications. Even if there are mild complications, like I say, a mild complication, fevers and no organism is identified, the patient just have temperatures, and that patient is doing well walking around their unit. But you don't want to send that patient home if they have a high temperatures. But in the absence of any significant complications, most of the time you spend two to three weeks in the hospital. Two, [00:43:00] we're talking about in the case of multiple myeloma, three to four weeks when we're talking about patients with leukemia, for the most part.

Marla O'Keefe: Someone was asking about how the success rates of transplants have increased over the last 10 years.

Dr. Tulio Rodri...: Absolutely. Yes, absolutely every decade, and there's some of several institutions have done that, but Mayo Clinic, when [00:43:30] they did a large analysis, especially with leukemia, every decade there's a survival increment. That's been said usually happen in younger individuals because those individuals are the ones that will go through transplantation more often. Fortunately now we have patients with, as I said, 27% of them even older than 65 years old, can go through transplant and most of them they do this effectively. Now, I don't want to minimize the advancement that have been achieved [00:44:00] with standard therapy. We no longer have only chemotherapy. We have immunotherapies, et cetera, that are making an impact. But the bottom line is that yes, survival, continues improving and it's not like it was five years ago, absolutely not.

Marla O'Keefe: So it continues to get better. Are there certain qualities, I guess it would be health or whatever, that would lead to the best results [00:44:30] in a transplant?

Dr. Tulio Rodri...: Yeah, I mean we use the triangle, or I use the triangle because that's something that I just made up, but in my mind the patient with a younger age, the patient with a disease that is in remission, and a good stem cell source, they have the best chance of an effective and positive outcome.

Marla O'Keefe: You mentioned a little bit about graft versus [00:45:00] host disease at the end of your presentation, and I know that not all patients get it. Are there some

common signs of side effects, and is there treatment that, are there things that you can do to maybe help prevent or minimize it?

Dr. Tulio Rodri...: Yes. So from the beginning, I mean we know that there's some risk factors. So depending on the age, the type of donor they match. So some of us might use different approaches. For [00:45:30] example, I remember several years ago using chemotherapy after stem cell was kind of a provision. Now, actually cyclophosphamide, cytotaxin, has been used after hypo identical transplant because they have a high chance of graft cell disease. So a few days after the fusion you continue giving chemotherapy to this individual.

Also, we have better drugs, and we have better drugs that have been tested in randomized tests like ruxolitinib [00:46:00] or jakafi. In the past we were doing many things out of desperation. There was nothing better than steroids. People were even pushing for, I mean nothing. So people were doing all sorts of things, putting central lines of extra corporeal for instance. Nothing against that, that the data on that is very weak. Very, very small numbers. Most of the trials were done in Europe. Most of those trials were using in [00:46:30] other drugs. Now we have drugs that have been tested in randomized trials and they have shown significant benefit in patient with a graft versus host disease.

Marla O'Keefe: Thank you for that. I have a few kind of more disease or diagnosis specific questions. Someone had asked is there any data on transplant for Richter's Transformation?

Dr. Tulio Rodri...: Yes. So it's not the most [00:47:00] abundant data because Richter's Transformation, for those who are not familiar, is when chronic lymphocytic leukemia conform into lymphoma. Why? So in chronic lymphocytic leukemia, we're talking about small cells that you might see in, a counterpart will be for literal non-Hodgkin lymphoma. But in this case these cells transform into diffuse large B cell lymphoma, different kind of lymphomas. And at the beginning people thought that that was not even possible. But [00:47:30] I can tell that I have seen a biopsy in where you see the lymph node and half of the lymph node is diffused large B cell lymphoma, half of the lymph node is CLL.

So Richter's Syndrome does exist, but it's not common. And of course at that point that usually requires stem cells. That transplantation has been done, it has been done effectively. And especially for adults who presented with more aggressive disease. Once they transform, usually that is a course, right? It's not going to behave like a standard regular [00:48:00] stem cell lymphoma. So yes, but again, this is not a replacement of your conversation with your physician. It's something that you want to discuss with your physician in detail as a general concept. Absolutely stem cell transplantation had been done, had performed in patient with Richter's Syndrome.

Marla O'Keefe: Thank you. Another question along those lines. Someone had chatted in, they have a sibling with down syndrome [00:48:30] that needs a transplant. Is there any data on transplanting a patient with down syndrome?

Dr. Tulio Rodri...: Yes. So I mean, I'm very sorry to hear that. Leukemias in down syndrome has been described. Many times we're talking about an acute lymphocytic leukemia because it is being diagnosed in an early age, and that's what you see more often in children. But AML, acute myeloid [00:49:00] leukemia, has been described as well.

One of the problems that we were having with transplantation in a patient with down syndrome is that appears to be too toxic. And interestingly, some of us years ago we were thinking that liver toxicity was going to be the problem for now that long toxicity. Pulmonary toxicity was higher than in comparison to other patients without down syndrome. That does not mean that cannot be done. [00:49:30] Like I said from the beginning, once you know what your side effects, you try to mitigate those in any way you can. Now, fortunately for ALL, and again, it's what we see more often, now there's other options like CAR T-cell. And again, none of these treatments, unfortunately, is 100% effective. But there is another option that we have for this patient. And there's an indication now for ALL, in the first [00:50:00] trials of CAR T-cell, there were some few patients who were enrolled and they had down syndrome.

Marla O'Keefe: Thank you. One last question. We have time, I think, for a couple more are, this is a vague one, generic one. Are visitors allowed in the hospital during the transplant process? Are the patients isolated?

Dr. Tulio Rodri...: No. Visitors are allowed. I mean, again, [00:50:30] I know several all programs, I'm not talking only based on experience in my program. And visitors are allowed. That being said, my recommendation is to choose one individual or two individuals. The higher the number of visitors, the higher the chances of having some infection. We had a patient a few months ago that someone came on a Sunday and then two days later, Tuesday, a friend, he called to tell the patient [00:51:00] he tested positive for COVID. Fortunately we tested him and he was negative, but just imagine. And he was asymptomatic when he was visiting. But now multiply that by 12 individuals who come to visit you. So your chances are going to be higher. So yes, it is allowed, but I'll strongly recommend you to select that single individual, no more than two individuals, who take their precautions before coming and visit you during that journey.

Marla O'Keefe: [00:51:30] Yeah, that makes sense. Definitely limit the contact. All right, we'll make this our last question. It kind of ties into something you just said about CAR T therapy and transplant. Are they, someone had asked about treatment for CLL, do you do transplant first, then CAR T? Or is CAR T something that's coming up or what's the thought process there?

Dr. Tulio Rodri...: Well right now we do our CAR T-cell therapy based on the data that is available, based on what has been published. And in [00:52:00] some indications you can use CAR T-cell after the first failure of your therapy. For example, that is the case of diffused large B cell lymphoma who fails a stem cell transplant or fail first therapy within one year, right? In follicular lymphomas, if those are relapsing within two years also. So depends on the timing and how many recurrences, or how many treatments, [00:52:30] that patient has required.

So I can tell you that right now there's no CAR T-cell approved for first line therapy, that you are diagnosed for the first time and you receive CAR T-cell. The sooner that patients are receiving CAR T-cell right now, outside of a clinical trial, of course, because there are clinical trial for CLL. Now they are developing clinical trial for AML. As a standard of care approved by the FDA, you need to fail one regimen. And is for the first [00:53:00] solve therapy that CAR T-cells can be considered in large cell lymphoma. So that is something that absolutely you want to talk to your physician. Obviously I always try to tell patients you need to empower yourself and you look for yourself and you bring your data to your provider. So I think that no one will be upset that you look for your data and you bring it for discussion.