Carrie Callas (00:01):

At this time, I would like to introduce our speaker for today, Dr. Kehinde Adekola. Dr. Adekola is an associate professor of medicine in hematology/oncology at Northwestern Medicine. Her research interests and expertise include stem cell transplantation and patient outcomes after transplants. She is also interested in cancer health disparities and global health outcome improvement, specifically in hematologic disorders. So I will turn it over to you, Dr. Adekola, and thanks for being with us.

Kehinde Adekola, MD (00:36):

Thank you, Carrie, for that introduction, and I'm very happy to have the opportunity to give this presentation. Today I'm going to be talking about managing graft versus host disease while living with leukemia. I like to start my presentation with this outline of where we've come from so that we have an ideal of how long we've been doing this for and all the changes that have happened over time. The first report of using bone marrow transplants, or I'm going to say it interchangeably with stem cell transplants was in the mid 1950s to 1960s, where basically we saw that there was a nation report for using bone marrow transplants as cancer treatment. And I guess what's relevant to this group is that we started doing allogeneic stem cell transplants in the late 1960s. And then for leukemia was early seventies when we started doing bone marrow transplants.

(02:13):

So in the late 1970s was when we first recognized that there was a human graft versus leukemia effect, but we also realized that patients had very bad graft versus host with allogeneic stem cell transplants. It was a major thing to find out that we could use calcineurin inhibitors. Calcine inhibitors are things like tacrolimus cyclosporine to prevent graft versus host disease. And as time has moved on, we went from doing stem cell transplants, allogeneic stem cell transplants with related donors to unrelated donors in the early eighties. And we've gone on from doing full dose allogeneic stem cell transplants to doing reduced intensity stem cell transplants. And as you can see over the years, our increase in allogeneic stem cell transplants just keeps on increasing throughout the different decades.

(03:15):

So in the US we report all our allogeneic stem cell transplants to the Center for International Blood and Marrow Transplant Research. Over time we still do more autologous stem cell transplants than allogeneic stem cell transplants. But you can see that over the years the numbers just keep on increasing. So we have allogeneic stem cell transplants in blue, and then there's still the most common reason that people will get an allogeneic stem cell transplants in the United States. And this is all the CIBMTR data. The first bind in blue is for acute myeloid leukemia. And then the second most common reason is for an MDS myelodysplastic syndrome, myeloproliferative syndrome. And then the third most common reason is for an acute lymphoblastic or lymphocytic leukemia.

(04:22):

Over time, like I said, it used to be that we essentially did only match related donor transplants. But as you can see from the nineties up until now, we're now doing matched on related donor transplants, meaning that it's usually somebody who's fully matched to the donor but not related to them as far as they know by blood. And then we have haploidentical stem cell transplants, which is usually refers to a related half matched transplant, usually from a sibling or parent. And then we have the mismatched unrelated donor transplants. And as you can see, those numbers are still low, but we expect that in the next decade or so we're going to start seeing those numbers go up just based on current research trends.

(05:21):

So as of 2015, there were over 25 million people in the donor registry. The donor registry basically from multiple countries, multiple continent. And then there are a lot of cord blood banks in multiple countries across the world. So right now, at least until 2 20, the number of allogeneic stem cell transplants for acute myeloid leukemia essentially varies depending on the donor. Again, we're talking about matched related donor transplants, matched unrelated donor transplants, the haploidentical stem cell transplants, the mismatched related donor transplants and cord blood. So you'll see that the blue line is the match related donor transplants. And you can see that as the matched unrelated donor transplant, which is the orange line, has increased, the match related donor numbers are going down. And it's just because there are more people in the registry, which is great. And you'll see that most people in the registry actually young now. And we don't usually have older individuals in registry, unless they went into the registry when they were much younger.

(06:43):

And then this is for acute lymphoblastic leukemia. And again, you can see that the same trend we are now having more matched unrelated donor transplants, then we have match related donor transplants done annually. And why does it matter? Because we know that stem cell transplant survival has essentially improved over the years. These are three lines. They're looking at three different time points. The black line is from 1993 to 1997. The blue line is from 2003 to 2007, and the red line is from 2013 to 2017. These charts, the line chart A, is telling us the probability of survival. If you look at the black line, the probability of survival at one to five years after stem cell transplant, if you got a stem cell transplant in 1993 to 1997 was much more decreased compared to the red line in 2013 to 2017.

(08:00):

And the reverse is what you see on the second chart, which is the probability of non-relapse mortality, meaning dying from a complication that's not related to the actual leukemia. And you can see that that probability has gone down over time. It means that if people are living longer with leukemia, then it means that people are more likely to have long-term complications of going through a stem cell transplant process, and that means chronic graft versus host. There are more people living with chronic graft versus host disease than there were in 1993 to 1997.

(08:45):

So it would be remiss of me to just talk about chronic graft versus host disease and not talk about acute. I'll just briefly talk about what it means to have acute graft versus host disease. So historically, or when we talk about classic graft versus host disease, or acute graft versus host disease, it used to be defined by a specific time point. So the 100 days max. So if an individual had acute graft versus host disease before 100 days after the stem cell transplant, it was deemed acute graft versus host disease. And if it was 100 days or more after it was deemed chronic graft versus host disease. But we now know that that's not true. There's no arbitrary line that says this is happening. But invariably, when you talk about classic acute graft versus host disease, it means that you're referring to this old way of classifying graft versus host disease. And it just means that the individuals developed in three organs, the skin, the liver, the gastrointestinal tract.

(09:52):

So mainly they developed most likely a red rash. They had maybe nausea, vomiting, diarrhea, and/or had abnormal liver enzymes or developed jaundice, yellowing of the eyes, yellowing of the skin before 100 days. But now we know that it'll cause acute graft versus host disease can actually occur after day 100. It could be persistence, meaning that it's crossed over from before day 100 to beyond 100 or it's

recurrence, meaning that an individual had acute graft versus host disease, it was controlled, but then they had a flare of acute graft versus host disease and it was after the 100-day mark. And then there's late acute graft versus host disease, which just means that this is the first episode of getting acute graft versus host disease, but it is after 100 days.

(10:49):

And what I typically tell people is, if you don't get graft versus host disease within the first 100 days, that's great. It's less likely that it's going to happen as time goes on as you get to six months as you get to one year. But people are still going to have, can still have acute graft versus host disease after that 100 day mark. And the incidence of this is 30 to 50% if a patient gets a match related donor transplant or it's or a matched sibling donor transplant and that's any grade. So mild graft versus host disease versus severe graft versus host disease. And that's why having a full match versus the mismatch matters because it kind of decreases the likelihood that an individual is going to have graft versus host disease. So we typically quote for an unrelated donor stem cell transplant, we quote this 30 to 50% risk of graft versus disease would go up to about 50 to 70%.

(11:53):

But again, that's any grade. I'm not talking severe life-threatening graft versus host disease or graft versus host disease that affects quality of life is usually, depending on whose paper you're reading, is usually in the realm of about 10 to 30%. So the Glucksberg Criteria will stage acute graft versus host disease, and it's again, typically when we think about classic acute graft versus host disease, it's usually three organs, the skin, the liver, the gastrointestinal tract. There's this stage where it's from stage zero to stage four. And for stage zero there's really like no rash. The liver is less than two milligrams. When they check the liver function test, the bilirubin test and the nausea or vomiting, they might have a little bit of nausea or vomiting, or the diarrhea could be very small. And at the other end of the spectrum of stage four and a patient has generalized redness or they could form little blisters on the skin like breaks in the skin if it's skin graft versus host disease and liver, the bilirubin is very high, usually greater than 15%, 15 milligrams per deciliter.

(13:09):

And in the gastrointestinal tract, there can be severe cramping or sometimes the bowels just stop moving things out, which we call an ileus. We stage the graft versus host disease and that allows us to grade the graft versus host disease. So you'll see that grade one is for example, only has skin involvement. So stage one and two skin involvement is grade one. And then once you start getting to stage one of the GI tract of the liver, then you start getting to grade two graft versus host disease. For chronic graft versus host disease, it's a multi-system immunologic disorder, so affects many organs in the body. It remains the leading course of late morbidity and mortality, meaning that just basically people feeling unwell or dying as a result of going through a stem cell transplant. And like I said before can occur in 30 to 70% of patients, it usually starts later than graft versus disease, about day 100.

(14:17):

But again, that's an oversimplification because there's no stop line where the body just recognizes that I should be acute graft versus host disease now because I'm less than day 100 and I have yet crossed that 100 threshold. And the mechanism, unfortunately even after so many years of doing stem cell transplants, it's still not well understood. There are different hypothesis as to why people develop graft versus host disease. Is it's induced by the donor T cells? Is there impaired T regulatory function? Is there an imbalance or dysfunction between T and B-cell homeostasis? So a disruption in the equilibrium of T and B cells. And we now know that chronic graft versus host disease can develop on its own just out of

the blue, de novo and doesn't necessarily have to follow an episode of acute graft versus host disease. It can follow after an individual previously had acute graft versus host disease or just basically an extension of a patient who's had acute graft versus host disease and then just has features of autoimmune diseases.

(15:42):

So there's certain autoimmune diseases that affect the lungs or affect the skin. For example, people who have skin tightening a condition called scleroderma, which is we know as a classic autoimmune disease. But then that's the way graft versus host disease presents in people who... Is one of the ways it can present in people who have skin chronic graft versus host disease. So the risk factors for developing chronic graft versus host disease are many, again, previous acute graft versus host disease. So the likelihood of getting chronic graft versus host disease increases if a patient has had acute graft versus host disease. The age of the patients. So older patients are more likely to have graft versus with host disease than younger individuals. If the patient is getting a HLA mismatched donor, whether it's related or haploidentical donor meaning a half matched transplant or an unrelated donor there is that increased risk of getting graft versus host disease.

(16:48):

If there's a gender mismatched graft like a female to male donor recipient situation, then that can increase the risk of graft versus host disease. If a woman has had multiple children, it can increase the risk of graft versus host disease for the patient. Anybody who has a history of acute inflammation, so anything can cause acute inflammation like an ongoing infection, pneumonia. Those kind of things increases the risk for developing chronic graft versus host disease.

(17:24):

Again, chronic graft versus host disease can be classic. So classic again is referring to that historic definition of greater than 100 days. But then now we know that there's the overlap syndrome where there features of chronic graft versus host disease and features of acute graft versus host disease in the same individual. And the key is early recognition. And this is where we rely on patients and their caregivers because usually if this is happening three months down the line or six months or nine months down the line, the physician is sometimes not the first person to notice because by then the hope is that the clinic visits have started to space out. So you're not seeing your physician as frequently as you were during the early transplant period.

(18:19):

So we want to, in addition to your regular visits with the physician, family members are usually the ones who might notice something different. We need to basically be more, I think patients need to be a little bit, maybe a bit more in tune with changes that are ongoing in the body because sometimes they could be very, very mild changes. I've had patients show up to my clinic who I'm the one who notices that there's a change in the skin and they haven't noticed. So sometimes these changes can be really, really mild or very slight.

(18:57):

There's the 2014 diagnosis and staging watch work group by the NIH consensus criteria. You can see four tables here. There's the organ or site of involvement which is looking, and then there's the diagnostics. There's some things that you see and you're like, "Okay, this is definitely graft versus host disease." So it's enough for you to say that an individual has developed chronic graft versus host disease. And then there's some that are distinctive, but they can be seen in chronic graft versus host disease. But using that alone to make a diagnosis of graft versus host disease is not ideal because patients can

develop other medical problems that are not related to going through a stem cell transplant. And then there are other features that people can have or common things that can be seen.

(19:52):

So say for example in the skin, I think the most common one that patients might be familiar with is when people have sclerotic features. So sclerotic features are similar to the disease I was talking about earlier, scleroderma where people can have skin tightening. I almost think about it as an individual having Botox on a place of, usually you have Botox on your face, but maybe you start having signs, the skin is more tight on other parts of the body like the arms, the belly, the legs, then people are more in tune with that. It's difficult to move their joints.

(20:32):

Then you start noticing that there's a little bit of tightening of the skin. But then there's, are there other changes - morphea like features. So you'll see that we are very good on having our patients see a dermatologist. We essentially want our patients to have a total body skin exam because sometimes you don't get that examination at your physicians, your hematology, oncology or stem cell transplant physician's office. But if you're seeing a dermatologist at least annually, then they pick up on these little slight changes in the skin. Changes in pigmentation, lesions on the skin, growth of lesions. Other features are things like the change in the sweating pattern or people have things like what we call keratosis polaris, where they're just little small dots on the skin. Almost like when you go out on your [inaudible 00:21:31] and you start to have goosebumps, but these goosebumps don't go away.

(21:36):

And then there could be redness, there could be rash, there could be itching. In the nails you see that there's no diagnostic sign of chronic graft versus host disease in the nails, they're distinctive signs. But you have to make sure that there are no other reasons because other things can cause these changes, new medications and infection. So you kind of have to just have a high index of suspicion but also rule out other things. There's scalp and body hair changes. In the mouth, the diagnostic findings is when people have lichen planus like changes. Which is kind of like whitish, I almost like whitish lines or whitish plaques in the mouth. Other findings could be dry mouth or they have little bubbles under the skin ulcers in the skin. In the eyes, dry, gritty, painful eyes.

(22:26):

Other things could be sensitivity to light, changes in the color around the eyes. And then in the genitalia women can have vaginal scarring and men there could be scarring or narrowing of the urethra. And then in the GI tracts, diagnostic finding is where in their esophagus there's almost like a web and it's difficult. People start finding it difficult to swallow or they have strictures or narrowing in the throat. Those are classic findings of graft versus host disease. But then there are other things that are non-specific. Anorexia, nausea, vomiting, diarrhea, weight loss. So you have to rule out other reasons why this might be happening before you chalk it down to chronic graft versus host disease. And then in the liver is the same thing. We're looking at the abnormalities in the liver function test, but again it's important to rule out other things that might be contributing infection autoimmune or immune problem or a new drug that was just started.

(23:37):

And then for the lung, ideally what you want is to get a biopsy and so you get a biopsy and a diagnosis that an individual has bronchiolitis or [inaudible 00:23:48] that's tells you this is diagnostic of graft versus host disease. But the thing is that sometimes not everybody's able to get a lung biopsy just because of everything else that might be going on. So it is something that you know kind of work closely

with other specialties to kind of come to that agreement that this is definitely chronic graft versus host disease. So the muscles that can be inflammation, joint stiffness, what we call contractors. In the blood system again, this is somebody whose blood counts may not even have recovered fully from stem cell transplant. So you have to have a high index of suspicion if you start seeing that maybe the eosinophils are high, the platelets are low, the lymphocytes are low and they have other symptoms. So you kind of tie everything together.

(24:44):

And the other category is the group I don't necessarily like because there are things that you can't explain many times. If people have new accumulation of fluid around the heart, in the lungs, in the belly, they have a kidney dysfunction, then it's not clear if this is not classic graft versus host disease. But these can be graft versus host disease. So the idea is trying to rule out other problems. And once you've been able to rule out everything, then we come to the conclusion that this is most likely as a result of chronic graft versus host disease. And what we're trying to do is once we determine that an individual might have chronic graft versus host disease.

(25:27):

So there's the NIH scoring criteria is essentially you assign the sites a score. So there's the performance status of the patient, it's looking at the skin, the mouth, the eyes, the gastrointestinal tract, looking at the liver, the lungs, the joints, the genital tract looking to see if you have symptoms. And it's a combination of symptoms and tests. So in the lungs a combination of symptoms and the regular pulmonary function test that patients get. In the liver symptoms and also their blood tests. So we use all these things and then we decide if people have mild graft versus host, chronic graft versus host disease, moderate or severe.

(26:12):

Usually when it's mild a patient has just one to two sites that are involved and the maximum score is one. And then if it's moderate, it means that they have greater than three sites that are involved or they have the maximum score is one or they have one site and the maximum score is two. But any lung will be considered, whether it's scored one or two will be considered a moderate. And then severe chronic graft versus host disease is usually if there's greater than one site involved or the lung is involved and the score is greater than two. But why do we really care about number of sites that are involved and the scoring criteria? Because we know that it affects our patient's survival. There's data to show that the two-year overall survival basically decreases as you go from mild to severe chronic graft versus host disease. For the mild, if it's mild chronic graft versus host disease it doesn't necessarily... Most patients are alive at two years after the diagnosis.

(27:35):

And then for moderate it's 86%. And you can see that once it's severe, the number really goes down to 62% at two years. When we're trying to treat graft versus host disease, the goal of treatment... Because when patients go through a stem cell transplant, the bottom line is the idea is that you want them to be alive, you want them to be free of disease and you want them to be living their best life. You don't want them to be dealing with complications or with a decreased quality of life. So what we aim to do with chronic graft versus host disease when we want to treat is, we want to decrease symptom burden reduction. We want to improve quality of life, we want to prevent the progression of the graft versus host disease and inflammatory activity. We want to prevent fibrosis, essentially scarring and disability prevention and preservation of response so that you can also withdraw immunosuppression because

the treatment of graft versus host disease is usually more immunosuppressive. And then you want to repair them and modulate the immune system and overall improve chronic graft versus host disease.

(28:51):

So treatment for graft versus host disease, the mainstay still remains our first line of treatment in 2022 are steroids. So depending on the severity of graft versus host disease at diagnosis of chronic graft versus host disease are your physician will decide what dose they feel like you should get in terms of steroids. Depending on how the patient presents, if it should be steroids by mouth or steroids given through intravenously. And what you want is that you want to see a response to the steroids and hopefully quickly because that's going to usually we like it if graft versus host disease responds to steroid pretty quickly. 'Cause one thing you don't want to see your patient go into this steroid refractory graft versus host disease group. But the beauty is that in 2023 we now have treatments for chronic graft versus host disease.

(29:56):

So when I first started doing this, we didn't have any approved agents apart from the steroids for chronic graft versus host disease. Which is hard to believe since we recognize this phenomena like years and years ago. If you go back to the previous chart that I showed you. So it's amazing to me that we got to 2017 and the first agent apart from steroids that was approved for graft versus host disease was approved and this was ibrutinib. And you can see that it was approved after failure of one or more lines of systemic therapy.

(30:39):

And then after ibrutinib, a bunch have come in succession. There's ruxolitinib, Which is essentially after failure of one or two lines of systemic therapy in both adult and pediatric populations greater than 12 years. And then the most recent agent is an agent called belumosudil, which was just approved in 2021. And again it's for people with adult and pediatric patients greater than 12, who have chronic graft versus host disease and have failed at least two prior lines of systemic therapy. And then there's site specific treatments. So if we go back to this table on the skin, we do topical creams for steroid creams. Some patients may have to get light therapy or get extracorporeal photopheresis. For the mouth, we can use the steroid mouth washes as well.

(31:40):

And then also things to kind of basically simulate saliva, keeping the mouth moist. In the eyes, we use eyedrops, serum tears are used, sometimes some antibiotics are used. In the GI tract we can give local steroids to coat the gastrointestinal tracts such as the budesonide, beclomethasone. In the liver. We give in addition you give as ursodiol, which is essentially a medication that helps with sludging in the gallbladder area, but also great for our graft versus host disease patients. For patients who have lung graft versus host disease, you are giving things like steroid inhalers, bronchodilators, almost like you know would give asthma patients. And then in the genital area you can also give things like local steroid creams or suppositories that can be applied in that area. So there's certain things you can do to target different sites that are affected. And the beauty is that we have more treatments to look forward to.

(32:56):

It's funny how we didn't get any second line treatments until 2017 and now we have so many ongoing clinical trials that are looking at graft versus host disease both after failure of previous lines of therapy and also in the frontline settings. So in addition to steroids. I think in the next couple of years there's going to be almost hopefully chronic graft versus host disease will be almost like treating high blood pressure or one of these other autoimmune diseases, where you have multiple options to choose from

and you can essentially tailor your choice of medication based on other things that might be ongoing with the patient. It's important to monitor different organs after a stem cell transplant and get regular follow up.

(33:47):

And you can see on the National Marrow Donor website if the guidelines are there and how frequently you should get them because if individuals have graft versus host disease have been on steroids or they used total body radiation as part of their conditioning regimen, they have to be monitored more frequently. So patients, you have to look for cataracts. Exposure to steroids can cause that very frequently. And then at a point it'll be annually. And then you have to make sure that you see your dentist if everything is stable about six months, 12 months annually. Getting your regular pulmonary function tests, making sure that depending on what symptoms you have that you're seeing a cardiologist at least annually. And most people now will be plugged into a survivorship program.

(34:43):

A survivorship program is also helping you to keep track of all these organs and all these systems. They have to be monitored over time in patients who've had graft versus host disease or who've had a stem cell transplant for whatever indication. So these are just tables with the different complications that can happen, the procedures that should be done and the timing that they should be done. These they're guidelines, so they're not set in stone. They're going to be tailored to everybody's individual situation and when it makes sense. So I thank you for the opportunity to talk to you about this. Thank you to the Leukemia Research Foundation for inviting me and I will take any questions.

Carrie Callas (35:30):

Thank you so much. Dr. Adekola, it was very informative and it's very hopeful to know that there are so many new treatments that are currently being used and that are coming up very soon that can be used to treat GVHD. So we did have some questions submitted in advance when people registered. But we did have a few questions that related to the same topic. So I'll start with that. How long can someone have graft versus host disease? How long do people need to be worried about it?

Kehinde Adekola, MD (36:33):

So it varies, it could be short or it could be long. So I tell people that if patients get to three months, no evidence of graft versus host disease and it's great to get to one year, get to two years. Most people if they're going to develop graft versus host disease will develop it within the first one to two years after a stem cell transplant. But it is possible because you know how we talked about risk factors for graft versus host disease, and we talked about anything that causes acute inflammation. So any infectious process, what it usually will do, it can stimulates the donor's immune system. So people who never had graft disease maybe get a bad infection in the third year after a stem cell transplant and it revs off the donor's immune system. But for the most part, if people have no graft versus host disease at five years or so, they're most likely not going to have graft versus host disease and most people truly will develop it in the first one to two years.

(37:42):

The thing is, I think the other part of your question is if you have graft versus host disease, how long can it stay? So the unfortunate thing is that if for some people they're battling it, it could be indefinitely for the rest of their lives. Those patients are in the minority. People who are dealing with graft versus host disease for 10 years or more, they're in the minority. The majority of people, again before five years

should hopefully have it under control. Most people even sooner. But it can become... And that's where we go to the quality of life. It can be almost seen like, okay, now I have this new chronic condition, almost like now you have scleroderma or have high blood pressure. This is something that a patient has to live with for the rest of their lives. It is possible in some people.

Carrie Callas (38:38):

Great, thank you. Is there evidence to indicate that graft versus host disease is more severe in older individuals, such as people over the age of 70?

Kehinde Adekola, MD (38:53):

Yes. So there's data to say the age of the recipient increases the risk for developing graft versus host disease. And severity also, I think it also brings into context for other things, because it's why did they develop graft versus host disease? How sick was the individual from the graft versus host disease? So an older individual is going to find it a little bit more difficult to repair and rally compared to a younger individual. It makes the graft versus host disease appear more severe just because it's an older individual. So physiologically might not be able to put up as much of a defense as a younger person. So it can be more severe.

Carrie Callas (39:40):

Great. If your potential donor is a female sibling who is a full match, to what degree should one expect chronic graft versus host disease or is a non-related donor more desirable as a match? Is there anything with regard to your donor and the link to graft versus host?

Kehinde Adekola, MD (40:02):

So this question is, I think it depends on what school of thought as a physician you fall into. Because yes, the donor is 50 and has had three children, so there're risks, but it's a fully matched donor. So a fully matched donor decreases the risk of graft versus host disease, but then she has three children which can increase the risk of graft versus host disease. And then she's older, meaning that the stem cells might not be as healthy as a young unrelated donor. So when you get to that situation, you're kind of weighing risk and benefits of one risk versus the other. What's the risk of graft versus host disease with using an older patient who's had multiple children versus an unrelated donor who's younger, who's had no children?

(40:55):

So I tend to like younger donors, but again it's usually if they're less than 30, 31 that's what I mean by younger and they're unrelated. So I don't like it when the patient's sibling is in about that 50 range because I'm still like, "Fifties young." But once we get to 60, then I'm thinking, "Okay, definitely I'm going to go with the unrelated donor who has younger stem cells in their twenties." But this 50 year old is kind of like a gray area for me. And still I always just look at everything and kind of decide if I'm going to go with the unrelated donor who's younger versus the 50-year old who's older and has three children. So it's not an easy decision to make when you have those options.

Carrie Callas (41:44):

Got it. Okay. Is stress a major trigger factor with graft versus host disease?

Kehinde Adekola, MD (41:54):

No, but I think about it as if you have an infection that's a stressor. So maybe not stress as in financial stress or everyday stress, but stress that affects you physically. I feel just even getting the flu is a stressor. So that can make people develop graft versus host disease.

Carrie Callas (42:24):

We had a couple questions in the Q and A box that I thought I would cover now. One is I'm tapering off Jakafi and have started experiencing joint stiffness. What can I do to limit this condition?

Kehinde Adekola, MD (42:38):

So I tell people stretching, constant stretching, yoga, Pilates, that helps if you can incorporate that into your daily routine. But then sometimes it could also mean that your body is not ready to come off Jakafi. So it's that conversation that you're going to have with your physician as to whether or not you need to be... Because it could, again, chronic joint stiffness. It could be the chronic graft versus host disease and your donor's immune system telling you that it's not yet ready to come off. So you have that good discussion with your physician and decide whether we think this is the chronic graft versus host disease flaring or if just stretching and physical therapy is going to help like yoga, I guess.

Carrie Callas (43:30):

Great. Another one in the Q and A box about what is a good line of defense to not get graft versus host disease. Is there any way of preventing it?

Kehinde Adekola, MD (43:39):

So everybody gets prevention medications off the top. So they get calcine inhibitors. Now we are given post-transplant cyclophosphamide as part of the condition in regimen to decrease the likelihood of graft versus host disease. But there's really no way to say definitely an individual is not going to get graft versus host disease because sometimes you see a patient and you feel, oh, they're definitely going to get graft versus host disease and they go through the whole process and nothing happens and they're fine and their disease is in remission. There's no rhyme or reason as to why one person will develop graft versus host disease and another will not. It happens, it's the same way that sometimes you say you decrease the likelihood with a match sibling donor versus an unrelated donor. It doesn't mean that if you get a match sibling donor that you can't get graft versus host disease. It can happen. So yes, we give all the medications to try and prevent graft versus host disease, but there's no one thing fixes it all.

Carrie Callas (44:44):

Got it. Here's a specific question. The question is from one of our participants, "I've had oral and ocular graft versus host disease for 10 years. I still take prednisone daily and carry vizio lidocaine. It seems the oral is getting worse though I get weekly red light laser treatment. Should I consider some of the newer treatments? I'm 70 years old."

Kehinde Adekola, MD (45:13):

Yes. So it is, yes, in discussions with your physician, depending on the severity of graft versus host disease, how it's affecting your quality of life. Because we want you to be able to enjoy your foods and your meals. So if there's pain and discomfort, you might want to talk to your doctor about maybe trying

one of these other new agents for chronic graft versus host disease if the prednisone isn't working, the laser therapy isn't working. And your doctor will choose what he feels is appropriate for you based on everything else that's going on.

Carrie Callas (45:54):

Here's another specific question. "I'm very interested in any experience with being treated with rezurock. Is it a forever treatment or does it affect a cure? Right now it isn't approved for use payment for Medicare patients. Will it ever get approved?"

Kehinde Adekola, MD (46:14):

No, it's FDA approved. Remember, the FDA indication is after two lines of systemic therapy. So you have to have those therapies. And some insurance companies aren't, I guess Medicare, they want to see that you got those other therapies first and they failed before they pay for it. But yes, what we want is for the rezurock to cure. But like I said before, some people may have chronic graft versus host disease indefinitely and other people will be cured and there's no way to predict who's going to fall into that category. The question in the chart where the patient has had oral graft versus host disease for 10 years. We don't want our patients to have graft versus host disease for 10 years, but some individuals will. So in medicine we kind of never say never or never say always because we know that there's always a couple of patients that will not fit into that box.

Carrie Callas (47:29):

Great. "Will physiotherapy help my range of motion and strengthen my arms and legs?"

Kehinde Adekola, MD (47:38):

Yes. I like physiotherapy.

Carrie Callas (47:46):

Can you explain how ECP, which is extracorporeal photopheresis, works, and how often it should be done?

Kehinde Adekola, MD (48:09):

Well, it depends on the center that you go to. So essentially it's a form of light therapy. So think about basically what happens is your blood is kind of recycled, your patients are hooked up to the machine, the blood goes into the machine, it's exposed to ultraviolet light, and then essentially blood returned to the patient. So your hope is that you're depleting the T lymphocytes with that exposure. How often depends on the severity of graft versus host disease.

(48:42):

So at initial consultation with your stem cell transplant physician or sometimes at our institution with the dermatologist, you essentially come up with a plan and it's not the same for every patient what the plan is. And based on this plan, you could decide that a patient is going to get ECP twice a week, every week for three months. And then depending on response, then we start to space out how frequently patients are getting treatments. But it's also, it's very patient specific. It's based on response because usually these patients are on steroids. And what we've been trying to do is get them off the systemic

steroids. That's when we employ ECP. So the hope is that as they're getting the light therapy, that you're decreasing the steroids over time.

Carrie Callas (49:41):

And there was a question submitted in advance about treatments for graft versus host disease in the liver. Do you have any thoughts around that, specifically?

Kehinde Adekola, MD (49:52):

The treatments? It's the same. It's a diagnosis ideally is a liver biopsy. So for any organ, ideally you want to get a biopsy. If it's the skin, if it's the gastrointestinal tract, if it's the liver, it's the lung because the pathologic diagnosis confirms what you were already thinking by looking at the patient. So that's the definitive diagnosis. But again, we know that depending on the clinical scenario, some patients are not going to be able to get a biopsy just because it's not safe. But that's really how you diagnose liver graft versus host disease.

(50:30):

And then treatments are the same thing. The steroids we give ursodiol. The one that what helps with the sludging. We give the same thing, ruxolitinib. We don't have a lot to choose from [inaudible 00:50:45] and the ibrutinib. Yeah, so those are the agents for chronic graft versus host disease, but there are other agents that we can use. But we use them a lot in the acute phase than more than the chronic phase. Yes. And again, these agents have kind of come and I keep on wondering how did we practice stem cell transplantation before these agents came in? It just seems so like a cake or we used to use... Yes.

Carrie Callas (51:13):

Have you seen positive results of using red light therapy to help skin conditions?

Kehinde Adekola, MD (51:19):

In general, yes.

Carrie Callas (51:21):

Right. And it looks like that's it for questions. I guess we'll conclude with, first of all, thanking you, Dr. Adekola for taking time out of your day to share all of this great information with us. And to everyone here today, thank you so much for joining us and we hope to see you again in the future. Thanks.

Kehinde Adekola, MD (52:12):

All right, thank you. Thanks for having me.