National Bone Marrow Transplant Link
Chronic Graft Versus Host Disease: Latest Treatments & Advances, the Most Common Complications to Watch For, & Coping Strategies
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Presenters

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Q&A Participants

Webinar Ask A Question participants

Operator

Greetings, and welcome to today's nbmtLINK Webcast: Chronic Graft Versus Host Disease, The Latest Treatments & Advances, the Most Common Complications to Watch For, & Coping Strategies. At this time, all participants are in a listen-only mode. A question-and-answer session will follow the formal presentation. You may ask a question at any time by typing it into the Ask A Question feature on your screen. As a reminder, this conference is being recorded.

It is now my pleasure to turn the call over to your host, Jennifer Gillette. Please go ahead.

Jennifer Gillette

Thank you so much, Kevin. And thank you, everyone, for being here with us today. We are very excited about this webinar, and we hope it is just filled with information and support for you. Just a little outline for today's presentation. We will start with Dr. Trent Wang, who is an Associate Professor of Clinical Medicine with the Division of Transplantation and Cellular Therapy at Sylvester Comprehensive Cancer Center. And then we'll hear from Dr. Lara Traeger, a Clinical Health Psychologist, who is an Associate Professor of Psychology at the University of Miami and an Assistant Director of Clinical Research at the Sylvester Comprehensive Cancer Center.

And then we will hear from Michael Cramer. He is a T-cell lymphoma survivor, a son, a windsurfer, an influencer, and more, and he had a transplant and deals with GvHD today. And then, of course, we will have our question-and-answer period. Just a quick little intro. For those who have not heard of nbmtLink, we are dedicated to helping individuals and their families, from diagnosis through survivorship.

We work with hospitals, cancer centers, and other organizations to reinforce and complement medical care by providing resources, support, and education. If you decide to print these slides or come back to them, they will be on our website within a couple of days. And you can always just go to nbmtLINK.org to reach out to us.

Some of the resources we have are our Lunch & Learn programs that are monthly on a variety of topics. There is survivorship, disease-specific information, GvHD. We also have our podcast. We have 15 seasons with over 33,000 downloads. We have multiple webinars, and those are recorded and put on our website as well. We have blogs from those who have been through the transplant process, and again related to all kinds of information.

We have our Survivors Thrive Book Club, where you can meet with other community members and read some of those great books out there that are supportive and help you get through. We have our Peer Support Mentor Program for patients and caregivers, our Second Birthdays Recognition program. And we have a variety of materials and referrals that we can give you as well as our Facebook page, which is always action-packed and full of great information. A special thanks to our webinar sponsors, Sanofi, Incyte, and our esteemed Link partners, for we cannot do these programs without you.

Just a brief little introduction on making sure that you do not take any of the information from this program as specific medical advice for you. This is meant to stimulate conversation with your healthcare team. So now, onto introductions of our wonderful presenters here. Dr. Wang, as I said, is an Associate Professor and is in Clinical Medicine, the Division of Transplantation & Cellular Therapy.

He has been treating patients with cancers who require allogeneic stem cell transplants and other cellular therapy. His research focuses on complications of allogeneic stem cell transplants, including conducting interventional, behavioral, and retrospective studies for graft versus host disease, infectious transplantation complications, and survivorship. He also studies the effects of CAR T-cell therapy.

And Dr. Traeger is at the University of Miami and the Sylvester Cancer Center. She conducts patient- and family-centered research to enhance quality of life and quality of care among adults affected by cancer. Her work focuses on developing testing and disseminating strategies to enhance patients' resilience, health behaviors, and patient/clinician communication. She received her graduate training from the University of Miami and completed her pre- and post-doctoral fellowship at the Mass General Hospital Harvard Medical School.

And Michael. Michael is a 23-year-old cancer survivor, BMT recipient. He is a social media influencer and a motivational hero. A quick flashback. Michael was born in Paris but grew up in Miami Beach, and he has an older brother and younger sister. Michael was a surfer, skater, and on the Olympic development team for windsurfing. He traveled the world competing. And he was the funny one on the team, had his own style of water, made everyone laugh. He was full of adventure. And as a teenager, he had already experienced so much in life.

Unfortunately, his father died of cancer in 2016, and this brought the whole family together. Love and the ocean kept the family afloat. But then on July 14, 2020, tragedy hit again, and Michael was diagnosed with an insanely rare and aggressive cancer. And then--less than 200 documented cases ever. He has an average survival of eight months. But miraculously, four years later, he is still with us and doing amazing things.

He inspires others on TikTok and leads a support group for cancer survivors. And I want to tell you, we have just had such a pleasure getting to know Michael and his mother. And he has an amazing story that he's going to share with you. But I'm going to let him share some more of that story as we proceed today. And so now, we will go onto Dr. Trent. Thank you for being with us today.

Dr. Trent Wang
Hi. Good afternoon, everyone. I am here in Miami. Let me just get the slides to the right one. All right. Here we are. So today, I'm going to talk a little bit about graft versus host disease, or GvHD. I'm going to go through some of the background, our general approach as clinicians when we see patients with GvHD, what we're looking for, what we're trying to achieve, and some updates on the new, more promising medications and combinations that we're looking into.

All right, so the hematopoietic stem cell transplantation. I'm sure, just based on the audience that a lot of you all are familiar with this. But for those who are not, we do the transplants because we want an immunotherapy effect. And this immunotherapy effect is what we use to cure really advanced or bad blood cancers or bone marrow failure syndromes. The new bone marrow from a donor is essentially installed into the recipient and makes blood cells as well as immune system cells that protect us from infection as well as cancer.

A transplant is a very complex and rigorous process, as I'm sure we're all aware of. It's quite frankly a marathon. And how one does through the transplant process depends on so many things, including their baseline risk factors, how old one is, and their comorbidities, whether or not they have high blood pressure or weight issues, other medical conditions, as well as their support and lifestyle factors. They all contribute.

And once someone is eligible for transplant, they go through this pretransplant testing and treatment. If it's a cancer that we're dealing with, patients have had many rounds of chemotherapy or radiation already. And then after all of that, we bring them to the transplant itself, which often involves a month in the hospital. And they're treated with even more chemotherapy or radiation, a ton of medications that are often higher risk because they modulate the immune system, they are needed to protect us from infection, and so on.

And then, the hard part really begins after you go home from the hospital because then you don't have the nurse next to you whenever you need her. And there's a lot--a full-time job worth of medications to take, many visits, sometimes hours away from your house. And we have to deal with things that come up, including graft versus host disease.

So graft versus host disease is really--it's a part of transplantation. And it has been since the beginning. It's regarded as kind of a friendly fire because we want the graft versus cancer effect. That's what the new immune system is supposed to do. But, it has been not possible to extricate that effect entirely from the graft versus host disease. I have a picture. I made this in paint myself. It's a confused lymphocyte. It doesn't know what to do. This is an attack cell in our immune system. It knows it's supposed to get rid of bad things. But then, cancer is a bad thing.

But what about your skin? And what about your GI tract? Are those bad things, too? And it needs time to learn. So unfortunately, it goes through a learning process. And during that process, there is some damage done to the host's body. And there's two major types of acute and chronic GvHD that presents. Acute GvHD, which is not the topic of this talk, is something that is very common, happens within the first three months generally in the major organs, or the skin, the GI tract, and the liver. Those who get acute GvHD are a little bit higher risk of getting chronic GvHD, which is the one that happens after 100 days.

And usually, we tend to see it happen when we're lowering the immune suppression that was given during transplant. This is usually tacro or sirolimus. And sometimes shortly after stopping it, we notice that there might be mouth ulcers or a new skin rash or dry eyes that got worse or a plethora of other symptoms that can manifest. We have to distinguish between the two. They are very different in terms of how they're treated as well as how they affect the individual patient.

Chronic GvHD, to make light of the situation a little bit, is something that we have to live with. And I like to use the analogy that it's almost like that in-law, that parent-in-law that we're not super fond of, but we're married into the situation now. It's not going to go away quickly. You have to manage it. You have to learn to live with it and look forward, not backward, and do the best that we can to coexist, just because when chronic GvHD exists, it exists on the order of years, not weeks or months.

So, it is the most common complication after transplant. It affects about 30% to 50% of transplant recipients. Although with newer ways of doing the transplant, with things such as post-transplant cyclophosphamide and some of the newer medications that are coming onto the market, we seem to be getting better at reducing it. You can see in this little picture on the right, of how many patients have chronic GvHD diagnosed, that each time after a transplant that the number goes up by one year. It's almost 30%.

By two years, it's a little higher. But usually between two and three years is where we see that leveling off. So if you don't have it by three years, you're probably very unlikely to get it. And chronic GvHD is a major cause of problems after transplant. And once we have it, it represents not only the symptoms that it causes, but it represents a little bit of a disregulated immune system state. So we have to be extra vigilant. And you have to stick with the transplant team, if possible, to look for these complications.

So, how do we approach chronic GvHD? It's very much a balancing act because we know that the symptoms of chronic GvHD, whatever they might be, whether it's the ulcers, joint problems, pain, you name it, they can cause significant quality of life impact. They can cause even irreversible organ damage or infections just by, like I mentioned, the disregulated immune system state. But if you treat it, you can also go too far toward the treatment side and cause a weakened immune system and the side effects of whatever drugs that we use. Remember, everything has its risk and its benefit.

So, this all needs to be very carefully weighed for each individual circumstance. So, the first thing, the first possibility when we have chronic GvHD is what to do. And one of the most common things that we do is do nothing. We can observe it. If there's a mild case of chronic GvHD, oftentimes if there's very mild mouth symptoms or eye symptoms, and the clinicians don't feel like it's dangerous, you can just wash it, see how it responds. You could even just come back in a couple months, see if it gets worse. You could also do something, of course.

And then, doing something is broken down into two major categories again. You could do something kind of conservative, which is using a local treatment, a topical treatment. The examples for the eyes would be eye drops or mouth rinses for dry mouth or ulcers, creams for rash, for example. Or if the manifestations and symptoms are more significant or severe, we have to treat the entire body using systemic therapies.

These are the pills, the intravenous therapies. These are the ones that broadly affect the immune system to try to reduce this GvHD process in the whole body. And this balancing act is very important because we need to figure out what works best for each individual patient. This is taken from a 2015 review article. You can see that early on, on the left side of this curve, manifestations happen. You will have a flare of a system, and then we'll treat it, and then it gets better and better and better. But then, it will flare up again.

Sometimes the flares are caused because we are lowering the immunosuppressant medication. Sometimes they're caused because we're exposed to an infection or something that activated the immune system. But regardless, it flares. And then, we go through the treatment process again. But over time, we think that there will be clinical tolerance, and again, time is years, not months, and that there will be less and less need for immunosuppression. So, our job is to keep you healthy and happy while this time is progressing, while we're going towards that clinical tolerance.

So, talking about some individual organs, how do we approach the skin if we're getting complaints? Our main goal is to control the symptoms, right? And that applies to all the organs.

We want to prevent skin ulcers, infections from happening. We want to prevent tightening, which can lead to the infections and lead to restricted mobility and quality of life impact. And with chronic inflammation of any organ, but especially the skin and mouth, we want to prevent cancer development. So, this is cancer screenings with the primary care doctors, with the dermatologists, you name it.

We use a lot of these creams, such as the triamcinolone creams and others. There's a whole bunch of options now in terms of creams. However, I think the steroid creams are still the standard. They are the most affordable. There's a couple new ones, such as (inaudible) cream and protopic cream. Those work well. They're steroid sparing agents. Sometimes insurance gives a little bit more difficulty in getting access to them, but they're very good.

The eye is an organ that is very commonly involved in GvHD. Our goal is to control symptoms and preserve vision and prevent scarring. Eye drops are very, very frequently used. We use things such as Restasis early on to try to reduce the inflammation in the eyes, even steroid eye drops. One eye drop that's been getting a lot of attention recently in our circles have been this one called Miebo, which actually works by preserving the tear film on the eyes.

It is a prescription medicine. And there's also these lenses, the PROSE lenses, which is a prosthetic ocular environment, or something like that, lens. It basically traps tears as well and can help symptoms a lot. But, it has to be worked on with an ophthalmologist, so you do need to see the specialist for this.

In the mouth, we're trying to reduce sensitivity, pain. A lot of foods can cause symptoms. We're trying to reduce scarring in the mouth as well as tighten it. Some of you may notice that it's hard to open the mouth as wide as before. And that's because the tissues are getting tighter. Ulcers can happen. And with this chronic inflammation, again, the oral cancer development, mouth rinses are very effective.

The dexamethasone or steroid rinse can help with the red findings very effectively. Biotene and other rinses really help with moisturization. But overall, this is a very important organ because food has to go through this area. It needs to be controlled and really can cause a lot of morbidity if it's not. Frequently, the oral symptoms can improve a lot with steroids or systemic therapies and can improve quickly, too, so that's something we always keep in mind.

The GI tract, we want to make sure we're not losing too much weight, that there's no problems with swallowing or nausea. Weight is the best indicator for this, generally speaking, assuming other symptoms are okay. Same as others, we do our colonoscopies as indicated for cancer screenings by age. The liver is an organ that's hard to prove is related to chronic GvHD. The liver enzymes, those labs that your doctor checks all the time, they're always a little bit elevated here and there.

Frequently, it's from medications. Frequently, it's from other causes. It's hard to prove it's GvHD without a biopsy. But, when we see GvHD somewhere else, and the liver enzymes are constantly elevated, we start thinking it's the liver. The one enzyme we don't want is a bilirubin. If that number goes up, we take it very seriously. That can be very dangerous, so we have to treat that aggressively. But assuming it's the other, the transaminases, or called the AST, ALT (inaudible), we can treat those somewhat conservatively.

What we're trying to do is reduce inflammation in the long term. We're talking years. Because that can lead to ongoing liver damage. One medication we use all the time is this ursodeoxycholic acid, or ursodiol. This is used in some autoimmune liver conditions, but it works really well in transplant in reducing liver inflammation and calming down the liver enzymes. There is barely any side effects to this drug. Sometimes it causes itching, but it's very frequently used in our circles, and we like it a lot.

The lungs can be affected by GvHD. The most devastating manifestation would be a lung involvement if it makes the lungs not move air effectively. The lungs are supposed to take air in and push it out. And GvHD can make it so that the elastic fibers in the lungs no longer work well, so the lung gets trapped--air gets trapped in the lungs. And that's a problem. So, we have been observing lung function very closely in the recent years because we think that this is something that we need to identify early and intervene early.

Any change in shortness of breath warrants a call to your doctor. This phone booth, I made that picture myself also. I'm kind of an artist. But, the phone booth is a pulmonary function testing. And we do that every three months for the first year and then a little bit less the second year and just hope that it stays stable. Anything can influence it, including colds and infections and effort. So, it's a little bit hard to interpret but need to stay on top of that.

There's certain interventions we do, including starting antibiotics or inhalers that sometimes help to preserve that function if we see a decline. And sometimes, we give a course of treatment for it if we see a decline in the lung function. The joints, the fascia, the mobility of these things are very important. We want to keep all your joints working as intended. Physical therapy is very important but also just exercise on a regular basis.

In terms of the genital urinary GvHD symptoms, we want these to be as minimal as possible. There's a lot of hormonal shifts that happen with transplants. Some people go into a failure--ovarian or testicular failure afterwards, but we have specialized clinics that can help enhance sexual health and satisfaction, if needed. It's sometimes a hard conversation to approach with your providers, but you still have to do it. You have to bring up these symptoms as they arise. Don't be shy.

When treatment, and I'm talking systemic treatment, is needed, the standard of care is still steroids, corticosteroids. This is the prednisone. It works really well, at least initially. However, it's hard to stop them altogether because sometimes the symptoms get worse, as we mentioned. And the regimens are a little bit complicated. They want you to take 50 mg a day and then another dose tomorrow. And it changes every week. It's a mess, not to mention, the real dark side is all the side effects.

Steroids are really good at shutting down the immune system and causing all sorts of stuff, insomnia, weight gain, diabetes. Oh, my gosh, there are so many side effects. We cannot keep people on high doses long, but it's a necessary part of the treatment for almost everyone, at least initially. So, this is a problem. And fortunately, we're looking at agents that can help us reduce the steroid doses or hopefully in the future replace steroids altogether, although that's not here yet.

And this slide shows all the progress that we've made in the last seven years. Since transplant was kind of invented, so to speak, in 1957, there's been a whole lot of nothing going on in terms of the FDA until 2017 when suddenly we had four FDA approvals coming through this year. So, this is good news for everyone on this phone call, that we have plenty of things to look forward to. And we're only starting to learn how to use these drugs, either alone or in combination.

This is a very messy diagram. Someone said sound disappeared. I don't know if you can hear it. Can you still hear me right now? Hello.

Operator
Please proceed.

Jennifer Gillette
I can hear you.

Dr. Trent Wang
Okay. All right. Thank you. So, this diagram just gives you guys an idea of how we as clinicians approach the treatment. We know that chronic GvHD probably results from many different parts of the immune system acting up. And we have designed many different treatments that target different parts of the immune system, so the highlighted ones of belumosudil, the ruxolitinib, the ibrutinib. They target specific parts that we want to shut down.

Speaking of some of the specific agents, ibrutinib was our first approval. It was actually approved on a very small trial of 50 patients. This trial had a lot of people who had the red ulcers or red skin rash that generally responded really well to steroids as a whole, but they saw that this drug worked really well in abating those symptoms. The FDA approved it. It does have its share of side effects, including heart stuff, infection, diarrhea. It's not super commonly used. However, in many specific circumstances, like I mentioned, in oral or in someone who has had a history of chronic lymphocytic leukemia or a prior cancer that ibrutinib might target also, we would use this drug more.

Belumosudil, or Rezurock, was the next approval after two or more prior lines of treatment. It targets the scar-related pathways. They try to reduce scar formation and rebalances the immune system. It is one of our most commonly used drugs because of its tolerance. It seems to have very, very little side effects. And most times when complain of the side effects, we rechallenge them later, and then it doesn't come back. We put them on this very frequently, and it tends to work very well.

And ruxolitinib, or Jakafi, is another one that has FDA approval. This targets inflammation pathways. It was previously approved for myelofibrosis before this. And the benefit of this is it has the most data. It compared the Jakafi versus everything that wasn't Jakafi at the time, and it showed that it fared much better for those patients. The side effects for Jakafi are still pretty reasonable, well tolerated for the most part. Sometimes we watch the blood counts a little bit closely on initiation. There's always that risk of infection. But that applies to any GvHD treatment just because we're targeting the immune system, a very, very good drug.

And the newest one on the block that we don't yet have access to, but any week now, is axatilimab. This was approved a few months ago, targets another component of the immune system called the monocytes and macrophages. And this is different than all of the others because it's intravenous. It goes through the veins, so you will need IV access. On the clinical trial at the higher doses, it caused some side effects with liver enzymes or sometimes swelling around the eyes, not in the eye.

But, the dose that FDA approved, there were very, very few side effects. And in our experience here on the trial, we saw it very well tolerated. The benefit of axatilimab is also that people who were treated had been exposed to the prior medications that we just mentioned, too. So, this is going to have a lot of use as well.

I always make a mention to extracorporeal photopheresis, which is a blood exchange process, which targets the (inaudible) cells and promotes like a tolerance. This is very good. We use it for advanced cases. And it very rarely causes serious infections. The worst part of this treatment is the time commitment. It's twice a week for two hours to begin. And usually, we give at least a three- to six-month trial of it. So, that's the worst part of it. And you have to be near somewhere that does this treatment.

So, my closing thoughts, there is a lot of progress being made. There's a lot of new drugs. We're figuring out how to use those new drugs. A lot of centers are combining them. They're using them at different parts or for different organ involvements. It's a very tailored approach. Not every center does anything the same, actually. That's what we figured out. If you had five transplant physicians, you'll get eight opinions. So, we have plenty to work with these days.

What we need to watch out for in chronic GvHD is new or worsening symptoms. You don't want to hide things for two or four weeks before you tell the doctors. We want to make sure we're not missing infections as well as worsening GvHD. We don't want to miss out on physical or psychological symptoms here.

Don't forget, I mentioned the word cancer a lot, and we're not even talking about the original cancer for the transplant. But, health maintenance for routine cancer screenings, skin cancer, mouth cancer, colon cancer, breast cancer, cervical cancer, those are the important ones. You survived the transplant. Now you have to make sure you don't get a different thing, different cancer from it.

Always new treatments are in the market. Always look for clinical trials. Some people use the term guinea pigs. But, how do you think we got any of our new treatments approved? It is through the selfless work of clinical trials. We bring them here when we think there's very promising medications or combinations. I strongly encourage you to consider one. The worst part of a clinical trial oftentimes is the number of visits. It's a little bit more than standard of care. But generally, it's worth it, in my opinion.

And we need to focus on all the other elements of being a survivor, including the behavioral health, the survivorship. We need to work on getting all of this data and expertise available to everyone who doesn't live near a major transplant center. Digital health platforms or apps are something that we, along with Dr. Traeger, who is going to speak, has been working on to get this out there. And that is my last slide. Thank you so much.

Dr. Lara Traeger
Great. Thank you so much. I'm going to jump in. I'm Lara Traeger. And I'm really excited to be able to talk here about coping with chronic graft versus host disease. So before I start, I just wanted to mention that I haven't myself been through a transplant, but I've worked hard in my work life to research strategies, coping strategies that patients and families can use in coping with transplant survivorship in graft versus host disease. And we've done this work in partnership with a lot of patients and families, physicians, nursing staff, and other providers. And so, what I'm going to be presenting here today is some of our lessons learned.

The second thing I also wanted to mention when we talk about coping is that everyone listening to this comes with their own sources of resilience and the strategies that are already working for you. So, anything I talk about here today, hopefully something will resonate with you, reinforce what you're already doing, and maybe there's something new here that you can add into your back pocket.

Dr. Wang went through a lot of information about chronic graft versus host disease, and it reminds me of this quote here, which is where I wanted to start. So, this comes from one of the patients we've worked with before. And I use this quote a lot. "Managing chronic GvHD is my full-time job. You can't stop the medication, so you keep going like if you have a job that you didn't enjoy. But you need an income, so you keep going. This is my job." And I think about this quote a lot because it reminds us that coping with chronic GvHD is not just about managing the physical symptoms, but it's about optimizing our everyday quality of life.

So, I don't want to bury the lead here. These are my three main points that I'm hoping at the end of my part of this presentation, that these are some points you can walk away with. So, I'm just going to give them upfront. No surprises here. Dr. Wang mentioned, "Don't be shy." And I think that is such a critical point. And that's one of my first points. Staying informed about your health and asking questions about your concerns is essential to survivorship, so no shyness here.

Number two, by using a mindful approach to daily challenges, you can stay present in the here and now and accepting of what is right now, while also being more active in deciding what comes next for me. And then finally, number three, each person's experiences of life after a transplant are unique, yet survivors and families can support each other and learn from each other.

So, I'm going to dive into these three areas now. First, overall, I talk about coping, I talk about finding a balance between acceptance and change, so making a change when we need to and practicing acceptance when we need to do that. I think everybody here has a balance that they strike between finding a solution, working on a solution, and being able to tolerate what's happening now with not always being able to change something.

So, if you think about your own coping strategies, do you tend to be a fixer, a problem-solver? Do you tend to focus on making change? Or are you someone who tends to more sit back and take what comes? Every one of us has a style that we tend to use, and it really is helpful when managing chronic GvHD to always reflect on that balance that you're striking today. Is the balance you're striking today the right one? And there's always room for shifting.

So, here are just some quotes that we've gathered from the patients and families that we've worked with that help to illustrate this idea of sometimes needing to look back at our balance of making change and practicing acceptance and seeing if any shifts need to be made. So the first one on the left here, "If I'm rinsing my mouth four times each day, every single day, just like my doctor recommended, why do I still have some mouth sores and pain? What's the point? What's the point of continuing to do this?"

The second quote, "I avoid any place that might expose me to germs and infection. I mostly stay to myself at home. It's tough, but I think this is necessary." And then the final one, "It's hard to figure out when I'm going to be awake to take my pills, do my mouth rinses, and use the skin creams on time. How do I get it all done?"

So, you can see here different kinds of struggles. I don't know if any of these resonate with you or if you have other challenges that you face. But for any one of these scenarios, it's really helpful to look at that balance. Is there something that I could do? Could I reach out to my care team and ask them for more help or more ideas or more information? Should I take a step here? Or is there something that is--how much of this is out of my control, and I need to practice focusing on taking care of my emotions and taking care of how I feel?

Sometimes it's a balance of both. And it's always good to again reflect on the challenges you're facing today. What kind of coping might make sense here, and is a shift called for? If there is time for a change, I always say, "What in my life am I focusing on now that there might be time for a change? And can I make that change?" So, I would challenge everybody here to ask yourselves, what is one thing that you want more information about or want to take steps to change related to your GvHD?

And in addition to setting that goal of something you want to get more information about or change, think about these next two questions because they are just as important. The first one here is, what could get in the way of taking that step? And how can you address whatever is getting in the way? It's not enough just to set our goals, but we have to think about what could get in the way of them. And what do we have to do practically to get around those barriers?

So for instance, if you're getting the sense that you need to re-engage with something like physical therapy, you might already have some reasons why this is going to be hard to do. Maybe you're not sure if you can manage it, if you're too busy. You're not sure if your insurance will cover it. You're not sure if it will even help. So, any of these thoughts could get in the way of you moving forward. So, think about what will get in your way and how you can possible move around those barriers.

In addition to the change side of things, think about anywhere and what you're coping with from day to day. Is there room for acceptance? And the underlying question there is also, and can I tolerate it? Can I bear what I'm managing from day to day? So, whether or not there's more information to get or a step to take or a problem to be solved, we still need to sit with uncertainty in day-to-day life. We still need to sit with emotions that sometimes are uncomfortable.

So, we can't control every aspect of life, and you can't control every aspect of your life after a transplant, but you can manage how much fear or worry or anger or sadness or any of those emotions take the wheel or take the driver's seat and control your day. So, I'm going to focus a little bit more on that now.

What you see on this slide is a painting. It looks like a tree with some yellow leaves. You've got some shadow; you've got some light peeking through the trees. This is how I think about practicing acceptance, specifically of our emotions. I know Dr. Wang talked about the importance of caring for your behavioral health. And this is really coming to light here. So, what I mean by showing this painting here is that more than one color is available in this painting.

You've got shadows, you've got light, you've got darkness. It's just like feelings. More than one feeling occurs in our life at one time. You can feel happiness right at the same time you're feeling some sadness, and maybe happiness is prominent, but there's still some sadness or fear in the background. So, the benefit of acknowledging all these contradicting feelings is that it allows you to see that bigger picture in all its glory without sacrificing any one thought or feeling at a time.

So for example, if, let's say, you're attending a family event, and you're really happy to be there, but there's also something about your health that's got you feeling down, sad, or worried, we can acknowledge all of the feelings at the same time without having to force ourselves to just experience one of those and push out the other ones. When we try to push out our feelings, it doesn't work very well. We can acknowledge how we're feeling in all its many colors.

And if you want to focus more on your happiness because that's going to bring you more peace or more joy, you can shift your lens but not necessarily completely ignore all the other feelings that might be there together. The one thing that can happen is that it is harder to shift your lens to the feelings you want to be focusing on when some of those negative feelings are so intense. And after a transplant and as you're coping with GvHD, you might find that your emotions are more intense than maybe what you remember from before your diagnosis.

So, if you have these intense feelings that are pretty uncomfortable, like anger, guilt, blame, shame, fear, what I recommend is doing a little detective work and looking to see, are those feelings that you're having, those intense feelings that are hard to ignore, they're sticky, are they linked to some pretty rigid or negative thoughts? And I have some examples here, like, look what I've done to my family. I have no control over my health anymore. Since my transplant, everything is wrong.

These thoughts are pretty rigid, and they're not helpful. But, the other thing about them is that usually they are not accurate. And oftentimes, when we're in a better emotional place, we can push these thoughts out, we can be more flexible around them. But, there are going to be times here and there when they're harder to get rid of. And so when you find that these emotions are intense, think about the thoughts that are coming with them. And when you identify those thoughts, you talk about widening your lens. So, recognize that sometimes when we're stressed, our thoughts get really rigid, and we want to widen them a bit.

So, if we say, everything is going wrong, a thought like that, widening your lens means recognizing, you know what? Some things aren't going great. Some things aren't going like I wish they could. And at the same time, there are some things that are going okay. So, you're just not always being a Pollyanna, but you're just widening your lens to look at that big picture again. So, you can see the picture I have on this slide is this narrow focus that really takes out your view of that bigger picture in all its glory, with the positives and the negatives and the neutrals altogether.

The last thing I wanted to touch on is support. So, some of you may have had experiences, or you've gotten a chance to meet others with chronic GvHD, and some haven't. if you haven't, you may wonder, would that even be helpful for me? And so, you're going to hear Michael's story in a little bit, and you can start to, as you're listening to his story, think about how it's actually helpful to you simply to hear someone else's struggles and learn from them and be inspired by them.

So, here are some quotes from people who have worked with us in our research programs and done our supportive care programs, what it's like for them to be part of support groups with other people coping with chronic GvHD. So just as an example, someone told us, even if they didn't have the same symptoms, they knew the same struggles. Everyone thinks, oh, you're in remission, you know your cancer is gone, but they don't understand the things you carry with you, like how tired you can get, your eyes bothering you, or just the other things that go with it.

And someone else said, I'm extremely grateful that I got to share things with people that really understand. That's the best part. And then finally, I'm going through some decisions about my eyes with GvHD. And hearing people talk about their own experiences with that is helping me like just stay a little calmer.

And so, you can see here just some examples and just a suggestion to consider reaching out for support from others, either through local organizations, national organizations like nbmtLINK. Even your providers may have ways to connect you. But hearing other people's struggles and challenges and opportunities and successes and being able to sit next to them and bear witness to them, and also sharing your own, could actually be helpful.

We also know that there are likely family and friends on this call, caregivers, as we call them sometimes. There are things that you can do as well in terms of support. So, if you are supporting a loved one who is living with chronic GvHD, let them tell you what they need. We don't have to assume that they need a certain type of help. We can ask. Remain calm, and don't rush things.

Sometimes people don't want to process what's going on. They don't want to talk about it. But, they will in their own time. Expect a range of reactions. There are so many different feelings that can come up, gratitude, grief, resentment, joy, peace, sadness. Expect that range. And that is normal. Acknowledge that your loved one may continue to feel different emotions even well after a transplant, years after a transplant. Emotions can come in waves.

And then finally, remind them that there's no right way to cope with chronic GvHD. I know this is a talk on coping, but one of my points really is that there's so many different ways to cope. And if you see somebody coping in a way that you wouldn't, it might not be right for you, but it might be right for them. I also show here that sometimes when you're living with chronic GvHD, and you've been through a transplant, you still have so much strength and power to be there for your loved ones who are going through it, too.

So, I have here six ways that people living with chronic GvHD and their loved ones can support each other, by acknowledging what each other is going through, normalizing their emotional experiences of that, validating those experiences--those experiences are real, and they deserve attention--expressing gratitude when you can, when you're feeling it, communicating clearly.

Even if you've known someone their whole life, you can't expect to always know what they're thinking and feeling. We do have to ask. And we have to express what we need and how we're feeling and what we want. And then finally, advocating. If you see that your loved one could benefit from more care, more support, help advocate for that. So, I just wanted to thank you very much. And I'm going to pass this to Michael and his very inspiring story. I'm excited for all of you to hear it.

Michael Cramer
All right. Thank you so much, Dr. Traeger and Dr. Wang. You guys are amazing. Thank you so much for sharing. First of all, I'm so honored to be here. I'm very excited to share my story with you guys. And as you can tell from this first slide here, I was a surfer, I was a windsurfer, and I was an athlete. I was on the Olympics--was on the team for windsurfing. And spoiler alert, as you guys know, I was diagnosed with cancer, and I do live with chronic graft versus host disease. But initially, when I was first feeling all these symptoms, I had no idea what was going on.

It was the COVID lockdown, it was March of 2020. I was just feeling really tired. I was away from school. I got home from college. Colleges were closed, the beaches were closed, the gyms were closed, schools were closed. It was just a really weird time. And I remember feeling super fatigued. And for a few months, from March, April, May and June, I really just did not feel like myself. I was doing home workouts. I was keeping myself as active as I could. I was trying to do everything I could just to feel better. But, I started to really not feel like myself.

And I live in Miami, and it's very, very hot here. And in the morning, the sun would come in through my window. And I would wake up in this drench of sweat every single morning and be like, "What is going on? I've never had night sweats before. Am I sad? Am I stressed? What's going on? Why am I tired? Why do I have night sweats?" And really I had no idea of what was happening. I did not even think cancer. Cancer was like the furthest thing from my mind. I had no idea what it was.

My mom and I, we initially thought that I had COVID. We thought that maybe I was diagnosed with COVID, somehow that I caught it. And this actually led us to go to my doctor at the time. And we did some routine blood work. She saw me. She said I looked good. She said I looked healthy. And she was going to let us know when the blood work came back and that she was going to call us if anything came up abnormal.

And for some reason, I still wasn't thinking anything after the blood work. And she called us a few days later and told us that we needed to meet with a specialist at Nicklaus Children's Hospital. Because at the time, I was 19. But, she knew this doctor, Dr. D. (sp), at Nicklaus Children's Hospital. And they were very close. So, she recommended me to him. And I was able to get an appointment with him during all this COVID madness very quickly.

And I remember, I was actually driving to my friend's house that day to help my friend with something. And I had to turn around. My mom was like, "Michael, we have to go to the hospital. They want to meet with you today. The blood work came back. She wasn't too happy with it. But, this other doctor is going to do some blood work of his own, and we're going to see what's going on. We're going to figure this out."

So, I remember going to the hospital with my mom, still not thinking anything. I was just like, "Okay, for sure, I'm just anemic." Like I had googled my symptoms. And Dr. Google told me I was anemic. So that's exactly what I thought it was. I remember going to the hospital. My mom and I met with a doctor there. He did some blood work. And after the blood work, he asked me if I would spend the night in the hospital and do a bone marrow biopsy.

And when he said spend a night in the hospital, I was like, "What are you talking about? Like I feel fine. I'm just really tired. I have some night sweats. I'm fine. Can we just come back the next morning and do this bone marrow biopsy?" So, my mom and I, we came back the next morning. He said it was okay. We didn't have to spend the night in the hospital. We could come back the next day. So, we did just that. We came back the next day.

And I did the bone marrow biopsy. And I was at a pediatric hospital. So, in a pediatric hospital, they put you under anesthesia for a bone marrow biopsy. And I remember waking up from the anesthesia. And the doctor, the super-nice guy, Dr. D., Dr. De Angulo, he walks in, and he tells me that what I have is a form of leukemia or lymphoma and that what I have is treatable.

And immediately, as you can see in this photo, I had my port placed in the next day. Like right away when I was diagnosed, I spent the night in the hospital, and the next morning, they rushed me into surgery. I had my port placed in the next day. And I was going to start chemotherapy right away. They were like, "All right, we have to start chemo. We're going to be starting you tomorrow. We don't know your exact diagnosis, but whatever it is, we're going to start you on chemo."

And unfortunately, I was not diagnosed until August 3 of 2020. Because I had the bone marrow on July 14 of 2020. And my mom and I, we spent a week in the hospital here. And we had no official diagnosis. They couldn't figure out exactly what it was. And they were sending my labs and all my biopsies all over the country to places like MD Anderson and all these very, very well-known cancer institutes around the country.

And finally, on August 3 of 2020, after waiting three weeks, a very long three weeks, I got my official diagnosis and started treatment. I was diagnosed with hepatosplenic T-cell lymphoma, which is a really rare and aggressive form of cancer, a very aggressive form of lymphoma that attacks the liver and spleen. And it was really, really tough. I mean, as soon as I started chemotherapy, like within a week, I lost all my hair, I lost all my muscle, and I was told I was going to have this thing called a bone marrow transplant.

And I was a surfer, I was a windsurfer. And that was the hardest news to hear that I was going to have to have a bone marrow transplant. Because initially, the doctor told me that I would be out of the water for at least a year, and I would be in the hospital for four to six weeks. So hearing that I would be hospitalized for four to six weeks, be out of the water, and not be able to surf another year was devastating news to me. Because the reason why I had my port placed in in the first place was so that I could surf during chemotherapy.

That was my main goal was to try and be as active as I could during treatment. But, that was not the case. And I only ended up surfing once during chemo because of how intense the treatment was. And on August, sorry, October 27 of 2020, I had my life-saving bone marrow transplant. It was a very, very long procedure. I was admitted for over six weeks in the hospital. I had so many different complications. I had (inaudible) syndrome. I vomited countless times. I had a (inaudible) morphine. It was a really, really difficult process.

The bone marrow transplant is not something to be taken lightly. It's a very difficult procedure. But thankfully, the bone marrow transplant did its job. It got my cancer into remission, which was a huge miracle. And I made it out of the bone marrow transplant alive, and that was such a blessing in itself. It was a very painful, very long process. But, I'm so grateful I had the transplant. I'm so grateful I got treatment.

But, life after the transplant did not go as expected. As you can see in these slides here, there I am all the way to the left. When I was first diagnosed with GvHD, I developed acute GvHD, which, like Dr. Wang said, is GvHD that's within the first 100 days of the bone marrow transplant. And initially, it was in my GI and my skin, and I had to be admitted to the hospital, initially for just two weeks because I had to be put on total parenteral nutrition because I was having so many frequent bouts of diarrhea and losing weight at a rapid, rapid pace.

So, it was very dangerous, very severe. And then over the next two years, GvHD really became my life. It was cancer and then, boom, I was hit with this extreme punch of graft versus host disease that manifested early in my GI and skin and then became chronic. About eight months later, it developed very severely into my liver. And as you can see in the photos, more to the right there, you can see I was very jaundiced and very yellow. And in these photos here, it really shows you how bad my liver GvHD really was.

It was a really hard process. And like Dr. Wang said earlier, I was put on a lot of steroids, and prednisone specifically. And it was a really hard time. Living with chronic GvHD, I was in and out of the hospital for the first two years after my bone marrow transplant, given all kinds of treatments like extracorporeal photopheresis, immunotherapies. Pretty much every single line of treatment that was out there, I had went through and tried. And nothing was really working.

And it was a really difficult time. I went through a lot of depression, a lot of anxiety, a lot of hardships living with GvHD, being in and out of the hospital. It was not an easy time. But, I was with my mom through everything. And thankfully, I had doctors like Dr. Wang who were there for me and really helped me get better, and just so blessed to have such a great team around me. And it was hard to stay positive during all this. But, my mom and I, we were together. And we did a lot of fun stuff during this horrible time.

We did a lot of Instagram, TikTok, YouTube. We even started a podcast together. So, when I was not so sick, we would do the podcast. And we would do updates from the hospital on TikTok and Instagram. And we would post our podcast on YouTube. And that was a great way of coping for us.

But like we always say with GvHD, chronic means long term. There was no end date to treatment. There was no return to normal. I'm still doing extracorporeal photopheresis. I'm still taking pills every single day for GvHD. And I do live with chronic GvHD. It's not something that's easy to live with. It's very hard to live with chronic GvHD. But, there's been a lot of good things that have come from this in the community I've found, the people I've met, the experience I've had with doctors, with nurses. It's made it all so worthwhile.

And I've really chosen to look at the positive from this whole experience because it's just taught me so much. And here are some photos of me at ECP smiling there. This is at University of Miami where I do my treatment, and so blessed to get treatment. And like it says here, "It's a permanent in-between state." I'm in remission from cancer, but with GvHD, you're never really in the clear. You're always looking out for things. You're looking out for symptoms. Whenever I feel anything, I'm like, "Okay, I got to e-mail my doctor because this is not right."

But, there's also a lot of fun to life now because I realize that going through something like GvHD, you have to find ways to cope. And as I'm sitting here in my room, I wish you guys could see. My room is full of Lego. And Lego has been one of the biggest ways I've coped. I used to love Lego as a kid, and I love it now. And I am a huge Lego nerd. I even started a Lego YouTube channel. I started playing electric guitar. My mom and I started speaking.

And these are all things I've been able to do with chronic graft versus host disease because chronic GvHD, it really, really messes up your quality of life. And sometimes, you can't even leave the house. So, I found all these things to do that I can do from my house, like build Lego, play guitar. And it's just really been important to find something that keeps you going, find something that keeps life fun. Because when you're taking dozens of pills daily, you're going to the hospital for treatment, you really just--you want to find some normalcy in your life.

And it can be really hard with chronic GvHD. I can't go back to who I was before. I'm not going to be out there in the sun all day surfing and windsurfing like I was before. But, you have to move forward, and that's the biggest thing I think I've taken from all of this is life goes on. And it's a different life living with chronic GvHD. It really is. And it's a very difficult life. But, it's definitely one worth living because there's so many new treatment options out there.

There is so much hope for things to get better. And just don't give up. That's the message to you guys, for anyone listening who is going through chronic GvHD, is there's always advancements, there's always hope, guys. So, just remember that. And thank you guys so much for being here and listening to my story. And if you guys have any questions, I would love to answer any questions that you guys have.

Jennifer Gillette
Thank you so much, Michael. We appreciate how authentic you are and just how you share your story so freely to help others. I think that's one of the most beautiful things I noticed about you and your mom the minute we met you. You're really helping a lot of people. And as well as--thank you, Dr. Wang, and thank you, Dr. Traeger. But yes, we are going to get to questions now.

Kevin, could you remind everyone how they can ask their questions?

Operator
Certainly. If you're dialed in with a phone and would like to ask a question, you can press star, one to verbally ask a question. Or you could type your question into the Ask A Question feature on your screen. Once again, if you'd like to ask a question at this time, please type it into the Ask A Question feature on your screen. One moment, please, while we poll for questions.

Jennifer Gillette
While we're waiting for either question areas to be filled, I already have some, so I'm going to start. And it looks like some of our questions start medically. So, this one is aimed towards you, Dr. Wang. I know you spoke about Jakafi and some of the use with it. And I know you said it's only been around for a relatively short time. But, this person asks, how--what has been studied as far as the viability as it being a long-term approach? Or is it something that might be used for just a period of time, and then they have to go to the next thing?

Dr. Trent Wang
Yeah, that's a great question. Probably two parts to this question. One is, what is the long-term safety of the ruxolitinib drug? As mentioned, it was only approved for GvHD in 2021. But fortunately, we do have a lot of experience in the oncology field with it as it was approved for myelofibrosis much longer. There's at least 10 years of data from the myelofibrosis trials. People can stay on this drug for literally a decade, and it doesn't really seem to cause much in terms of long-term side effects.

Again, the blood counts probably are the things that bear monitoring in the myelofibrosis population. And the long-term risk of infection and secondary cancer is just--on any immune suppressant, not necessarily Jakafi, but those are the things that need to be monitored when you're on anything for a long term. So, I think there's not much hesitation in terms of staying on it for an extended period of time, based on what we see from other disease trials for Jakafi.

In terms of the long-term approach to treating GvHD, if you've been on one drug for a long time, that's actually a pretty good sign. It means it's not getting worse. There's at least stability. Or maybe it's even getting better. The tapering strategies to reduce immune suppression vary so dramatically from provider to provider that it's hard for me to comment on it. But, we do know that we don't want you to stay on immune suppression indefinitely.

So, if you feel like you've been on a therapy for an extended period of time, and you're doing very well, I encourage you to bring it up to your clinician and say, "Hey, what criteria should we make to see if we can lower this dose a little bit or try stopping this or that," and working on that in the long term. Remember that tolerance is something that will happen over years. And if you're on the treatment for three or five years, there's no guarantee that you still need that treatment going forward. It definitely warrants a little bit of experimentation to see what happens when you reduce it.

Jennifer Gillette
Thank you so much. And, Michael, I have a question for you. First of all, in case you are not seeing them coming in, lost of kudos and thank yous to you on your very touching presentation. But, this one says, Michael, I'm also living with chronic GvHD post-bone marrow transplant eight years ago. Your experience feels so similar to mine. And if I could still make tears, they would be flowing down my cheeks. My question is this, how do you find managing your energy levels and keeping a social connection with your friends when you can't do all the same things you did before?

Michael Cramer
Yeah, that's a really great question. Thank you so much for asking that question. And thank you for being here. I know hard GvHD can be. And yeah, it's difficult to manage your energy levels with GvHD and keep up social connections. It's kind of like you pick and choose what you can and can't do. And on certain days, I realize that I can't go out with my friends. Like a lot of my friends go out, and they'll go, and they'll drink, and they'll go to these raves, and all these things.

And honestly, I just don't go to those things that they do. And I tend to hang out with my friends once or twice a week honestly. And it's difficult now to keep a social life and social connections because a lot of times, people want to do stuff that's outside or go to the beach in the middle of the day and do all these things that I really can't do. But, you just have to find friends that are willing to be there for you and kind of do the stuff that you can do, too.

And there are a lot of things you can do with your friends. Like you can go to the movies, you can go for walks, you can do chill things at their house. There's still a lot of stuff you can do. And it's just about having good friends that are going to be willing to do stuff with you and understand there's a lot of limitations on your life. And it's a struggle because everyone has busy lives.

And as far as energy levels go, yeah, the energy level stuff is hard. I mean, I just got back to going to the gym. And I find myself very fatigued after I go to the gym. And it's not the same as before. But I think it's about understanding that every day, at least with me, I have like one big burst of energy I can put into an activity. And then for the rest of the day, I kind of lay low and do other things that are less stressful on the body. Because you need sleep.

And I try to sleep as much as I can because I need so much more sleep than I used to need. I sleep probably like 9 hours or 10 hours a night. Like I sleep a lot more than I used to. Like I would be fine if I slept a few hours before, but now it's very different. And I'm just wishing you all the best and sending you all my love. I know how hard GvHD can be. So, thank you so much for just being part of this webinar and being here.

Jennifer Gillette
Thank you, Michael. And I'm going to piggyback and ask Dr. Traeger, do you have thoughts on the fatigue and energy question?

Dr. Lara Traeger
I think that Michael's response is really helpful because, first of all, just being able to hear each other's experiences, and even if we don't have the perfect solution, is helpful. So for fatigue, what he's talking about in terms of recognizing your daily fluctuations in energy and matching your activities to those fluctuations is really critical. So knowing your own patterns of when you have your most energy and when you have your least, and pairing the most energy times with the activities you know you need to or want to get done is really important.

You can also decide that sometimes you might overextend yourself, knowing you're going to be fatigued the next day, but knowing that that next day you do have time to recover, whereas other times you might make different decisions where you're really careful on a given day to not overextend yourself, so you do feel good the next day.

Jennifer Gillette
Great. Thank you. And, Dr. Wang, do you have any thoughts because I know this is a common one we hear a lot?

Dr. Trent Wang
No, I feel what Dr. Traeger says. I think it's challenging and just working on it day by day works the best.

Jennifer Gillette
Yeah, I agree. I also just want to add, too. I know we have done some other programs on fatigue. And if you search it on our website, you'll be able to see some of the programs related to it. But, I know there's been some other things that have been discussed at times, too, like a study done at Mayo with ginseng over a eight-week period. You can even search that on YouTube and hear about the findings with that.

I know we've talked about Dr. William Redd's research with white light therapy in cancer patients, as well as--I know sometimes with some of the different survivorship clinics, like if there's special days coming up, even some people have talked about--and I'm not sure if they're still doing this, I should double-check that with you, Dr. Wang. But like if someone has, let's say, a family wedding, and they really, really are trying to have just a little bit of energy, sometimes there might be a little Adderall or things prescribed as well. Are you still seeing that, Doctor?

Dr. Trent Wang
Yeah, we use that from time to time. It sometimes is a slippery slope because as an upper you really like it. And then you may want more and more of it with unknown long-term consequence there. But for important life events, it bears discussion with your provider. They might be willing to do it. It's not crazy to think about.

Jennifer Gillette
Well, thank you, thank you. I know we have some other medical questions here, too. One writer has a question about, you mentioned a course of treatment for lung function issues. And this writer wanted to hear a little bit more of that. Could you elaborate, Dr. Wang?

Dr. Trent Wang
Yes. What I was mentioning earlier was when the pulmonary function test shows a decline in the FEV1, which is the amount of air the lungs push out in one second, a whole list of possibility comes up in our head, and we have to make sure that it's not an infection, first of all. So when we see that drop, we send you to the pulmonologist, we get a CAT scan, we ensure there's no reversible infection leading to these changes.

If that doesn't seem to be the case, we oftentimes start something called FAM, fluticasone, azithromycin, and montelukast, three drugs that have been in a couple studies shown to either stabilize the lung functions or sometimes even improve it. And depending on the institution, you might get started on a course of steroids, a burst of prednisone for a few weeks. There's also a clinical trial looking at Rezurock, which is belumosudil, in these early drops in lung function. We don't have any data from that yet, but I know the Harvard group is looking into this.

So, there's a lot of possibilities. But unfortunately, there's no right answer either, that it's very much individual provider-based kind of management and just hoping that we continue watching the lung function, making sure it doesn't get worse and worse, since that can be very devastating.

Jennifer Gillette
Thank you, thank you. This one is aimed towards Dr. Traeger. This writer asks, my son has chronic graft versus host disease and is quite depressed but won't get help. How can we as a family get him to reconsider this or support him?

Dr. Lara Traeger
So, I just wanted to wish you and your loved one well. This is a difficult situation. One of the hallmarks of depression is that you lose your motivation. And so, it's understandable that somebody who is feeling depressed isn't always willing or wanting or having the motivation to reach out for help. So, there may not be a perfect solution to this. But I would say is that one way to have this conversation is to talk with that person about what it is that they would want for their quality of life.

So working on depression, you have to be motivated for that. So, what could they get out of it that would mean something to them? What do they want to be doing that they currently can't because of their mood? So, that could be something like spending more time with a favorite person or doing a favorite activity. Little by little, any activity that they can do, even to just make the day better, might help lift them out enough to be able to set those goals and partnering that, or pairing that with, okay, treatment for depression actually can help you reach those goals that matter to you.

Jennifer Gillette
Thank you. This one I'm going to start with Michael but also Dr. Traeger or Dr. Wang. If either of you have anything to offer, please feel free to speak after Michael. This writer asks, are there specific GvHD resources either of you recommend, either online groups, websites, et cetera?

Michael Cramer
Yes. So, I've heard of GvHD Alliance, BMT Infonet, and like a lot of other--you could look up like GvHD support groups online. I know there's a lot of resources. I myself don't actually--I'm not actually a part of any of these because I've been kind of busy, but I do lead my own support group. If you guys want to get the information for that, I can somehow share it with you guys on Discord (sp) every week for cancer survivors. And that includes people with GvHD. So, there is a lot of resources out there. There is a lot of support. You just have to look for it. And I'm sure you can find it. And there are great resources out there.

Jennifer Gillette
Michael, can you tell people, too, about your information with your website and podcast and how they can get more information about you, too?

Michael Cramer

Yeah. So if you want, you can go to michaelreidCramer, M-I-C-H-A-E-L-R-E-I-D-C-R-A-M-E-R. I know it says Cramer here with a K, but it's with a C. And that's my (inaudible) you can message me, and I can send you the information for the group. Or you can go to the website my mom and I have, which is michaelandmomtalkcancer.com. You can go there.

Jennifer Gillette
Thank you. Dr. Traeger, do you have anything to add as far as resources there?

Dr. Trent Wang
I think the resources that Michael mentioned are really good ones, so nbmtLINK, BMT Infonet, Leukemia & Lymphoma Society. They all have different kinds of resources. And so, I would check all of them just to see what is calling to somebody, what's resonating.

Jennifer Gillette
Great. Thank you. This one is for Dr. Wang. Dr. Wang, we had a couple people write in asking, how is it that some people get GvHD, others don't? And is there any predictability that when someone is preparing for a transplant that they're more likely to get it?

Dr. Trent Wang
You guys are going to love this answer. It's luck for the most part. That is the biggest part of it. There's definitely a few risk factors that can predict whether or not GvHD develops. The most common risk factors are age of the recipient. Age of the donor actually has been shown to be a GvHD risk factor. The older the donor, the more GvHD and complications from transplant that we are seeing. So, there's a push for younger donors, if possible, these days.

The source of stem cells. Peripheral blood stem cells show more chronic GvHD than bone marrow, although that was before post-transplant cyclophosphamide. We don't know that that's necessarily true these days. As mentioned earlier, the presence of acute GvHD can predict chronic. If you get a donor lymphocyte infusion, those extra T-cells can definitely contribute to GvHD.

The physiology of GvHD development is anything that really activates the immune system. There's things called DAMPs and PAMPs, damage-associated molecular signals and pathogen-associated signals. So if you get an infection, that can stimulate GvHD. If you sustain injury or stress, even, that could probably do it as well. Vaccines have been known to cause it. Really, there are so many variables that have been associated with it.

But in terms of modifiability, pre-transplant, earlier--the younger the donor, reduced-intensity transplant, less chemo or radiation with a transplant regiment, which of course, makes a safer transplant, but the risk of cancer relapse is a little bit higher when you do that. Those are also implicated with less GvHD if you get less chemo.

That was a messy bunch of sentences I just provided, but there's a lot. And of course, the newest research on some of the stuff that we've been looking at it is biomarkers early on. So for example, we're doing a study where we're looking at day 14 blood draws of certain biomarkers and seeing if that can predict who will get severe GvHD, whether it's currently acute. And maybe in the future, we'll be able to better predict chronic. But yes, there are signals that we're learning more and more about that lead to this (inaudible) of who is getting it and who is unlikely to get it.

Jennifer Gillette
Wow. There's a lot of factors there. Another medical question here for you, Dr. Wang, is asking about--I've heard it can better with time. Anything you can share about the thought of the time factor with GvHD?

Dr. Trent Wang
Yeah. I really am a big supporter of that notion. And I have seen it. We had a guy here who had really bad sclerotic GvHD of the skin. His arms were woody. A knock on the closet, it sounded like that. And he was on treatment with a couple agents, but predominantly, he was on ECP for a long time. And the first few years I've known him, it was the same. And then kind of over the course of one or two years, his arms just softened up.

And I was like, what on earth is going on? We didn't change anything. If anything, we were tapering the ECP. And he was about maybe 12 of 14 years after transplant at that point. And then, he was just like, "I don't know. It's better." And then, I looked at him, he looked at me, and we were both happy. And that was a case example of that. It can happen. We've just got to keep you healthy until it happens.

Jennifer Gillette
Great perspective. Another medical here. I suffer from chronic graft versus host disease and recently have been diagnosed with MCAS. Are you seeing more of this diagnosis?

Dr. Trent Wang
I presume MCAS is the mast cell activation syndrome. So, the answer is no. That is very rare from chronic GvHD. The main--there's eight organs that we routinely attribute to GvHD. And then when it's not one of the eight, we look at the more rare stuff such as myositis, muscle inflammation, fluid inflammation, fluid build-up, even things like myasthenia gravis or these weird eosinophil or mast cell syndromes.

Those are very, very rare. And when you do develop it in the setting of GvHD, it's hard for you to ignore the temporal relationship. But, I'm not aware of data kind of linking the two directly, although it's very suspicious to see them together, for sure.

Jennifer Gillette

Thank you. And another medical here. This one is, I am post-transplant of a year and a half, but I've acquired bronchiolitis obliterans syndrome. My question is, what do you see coming in the way of research, finding ways to stop damage in the lungs due to BOS?

Dr. Trent Wang
Yeah. BOS is what we were mentioning earlier, too, with a drop in the FEV1 and the way that the air moves out of the lungs. It's like an acquired COPD, essentially. There is a lot of research in this. Unfortunately, none of the research is great. The new agents that we mentioned, the pills as well as the IVs, all show some degree of response but usually in the 20%, 30% range.

And sometimes the responses are just symptomatic, not necessarily a numerical response on repeat pulmonary function testing. The important thing is, how bad are the lungs? If the FEV1 is really bad, like 30% or 40%, and you're barely able to live out your daily activities, I would be hard stretched to believe that a medication will reverse that entirely.

Usually, we recommend getting consultation with lung transplant physicians just in case that is on the table. But for the most part, it's about preserving further lung function from getting deteriorated and worse. Combinations of medications don't really seem to reverse severe BOS, from what we understand right now. So, it's very much about keeping what we have and exploring lung transplantation if it gets to that severity.

Jennifer Gillette
Okay. Thank you. Kind of related here, too, one person writes, I was on the rux study, but it didn't work for me. And I was transferred to imatinib. I couldn't get that anymore, and now I'm on Rezurock. Do you know if there are good results with the PFTs or FEV1 numbers?

Dr. Trent Wang
Yes. I think Rezurock probably has the most numerical data for bronchiolitis obliterans syndrome in terms of stability or improvement. Axatilimab was the one that I mentioned, which has a lot of symptomatic improvement data. So, there are some--there's definitely elements of data supporting its use in bronchiolitis obliterans syndrome, but it really depends on how severe it is and reversing any potential contributors such as infection. Yeah.

Jennifer Gillette
Another question here about donor lymphocyte infusion success rates. Any thoughts there, Dr. Wang?

Dr. Trent Wang
Yeah. I'm reading this one. This is complicated. Donor lymphocyte infusion is when we want to give extra doses of T-cells to the patient because their chimaerism is low. The amount of donor versus host in the blood has too much host than we like. And it's given sometimes to do that. It's given sometimes when the cancer has overtly come back after transplant. The success rate of donor lymphocyte infusion is very hard to give you an estimate.

It depends on the disease. Some diseases are much more responsive to it, such as the more indolent diseases. CML, for example, chronic myelogenous leukemia, which we don't do so much of anymore, responds the best to DLI, whereas the AML and ALL diagnoses respond a little bit less. I think in general probably somewhere around 20% to 30% response rates from just DLI alone. But oftentimes, we combine it with other chemotherapy or targeted agents. It's hard for me to give an opinion there, but it still has its role in this day and age, sure.

Jennifer Gillette
Thank you. Okay. Let's see here. And, of course, we have many thanks to you, Dr. Wang and Michael and Dr. Traeger. And let's see here. Kevin, could you remind everyone how they can ask more questions if anybody has additional ones?

Operator
Absolutely. You could type your question into the Ask A Question feature on your screen. Or if you are dialed in over the phone, you can press star, one to verbally ask a question. Once again, please type any questions you have into the Ask A Question feature on your screen. One moment, please, while we poll for further questions.

Jennifer Gillette
And regarding the chimaerism, is it true not every post-transplant person is 100%, many surviving with sub-100%? Do we ever see chimaerism decrease and relapse not occur?

Dr. Trent Wang
This is more of an anecdotal question, I guess. Usually, we want the chimaerism to be 100%. The cases where it isn't 100% early on is when we give a reduced intensity transplant such as very weak conditioning. And then, it can result in a mixed chimaerism for long periods of time. But, we generally see that over months to a year or two, the chimaerism tends to be full again. So, I'm trying to remember if I can find any cases where it was not full in the long term without relapse. I can't really think of too many.

Certainly, if the chimaerism is worsening at a point beyond 6 or 12 months after transplant, it would cause a further workup. And it depends on the disease for which it was treated for also. So, it bears cause for concern for the most part. But yes, theoretically it is possible that you can have a mixed chimaerism and not relapse. So, I guess that is the answer--the long-winded answer.

Jennifer Gillette
No, we appreciate all your answers, Doctor. And as we--I do have to ask, Kevin, is there anyone in the queue waiting to ask a question?

Operator
Not at this time.

Jennifer Gillette
I have a couple questions as well. Michael, sometimes we have people on this call that are preparing for a transplant, and they hear the word GvHD, and they want to know more about it. For someone who might be starting this journey, any advice to them?

Michael Cramer
Yeah. The biggest piece of advice is it's so overwhelming hearing all this, all the possibilities that can happen after transplant, all the things to worry about. But, I think it's really important just to focus on getting through. Like take it like day to day. Everyone always says take it day by day. But, you really have to take it day by day and just see how you feel. Because there's so much information when you're getting a transplant, when you have that meeting with your doctor, and he explains everything to you about the transplant and says, these are the possible side effects, this could happen, this could happen. It's so hard to hear all that.

But, you don't know what can and what cannot happen. Like there are so many things that can happen, so many things that can go well as well. So, you might as well go into it with a positive outlook and just hope for the best. And my biggest piece of advice is try to go in there before--if you feel up to it, like try to go in there eating a lot of food before, if you can. And try to exercise a little of the days before your transplant, the days before you're admitted.

Go in there as strong as you can, and try to get things to bring to the hospital that can keep you a little occupied. Bring your computer. Bring like something to do. Because during that time, you're going to be sick for a big portion of it. But, there's also going to be a portion where you're going to be a little bored if you start to feel better soon. So, just take it day by day. Don't be too hard on yourself. And don't worry too much about the future because that time will come. When it comes, easier said than done, but yeah, just take it day by day. It's a long, long process.

Jennifer Gillette
Wisdom beyond your years, and I know you earned every piece of it, sir. I have another question for you. As far as trying to help caregivers understand preparing for something like this, I know your mother was your caregiver. But, is there any recommendations you can make to caregivers on what help that your mom did or what things you guys learned along the way you might have to do differently?

Michael Cramer
Yeah. There's a lot. I mean, as a caregiver, it's very stressful to see the one you love go through so much and go through so much pain. But, I think it's just really important for the caregiver to know that there's nothing you can really do to take away their pain, but just be there for them. If they want anything--like if they want to eat like whatever food it is, you say, okay, whatever, you can eat it.

Because at that point, you just need nutrition. So, it's really just important as a caregiver to be there for them. Just listen to them. Listen to them, be there for them. Anything they want to do, they can do, try to help them do it. It's really different for everyone. But, my mom was very, very helpful.

Like she put on these like white noises in the room when we were there and very relaxing sounds. And that really did help when I was sick and just resting. So, it's different for everyone. I don't have any answer that's going to be perfect. I'm not a caregiver. But, I know my mom was just great because she was just there for me as much as she could be. So, just be there for the one you love. And that's really my biggest piece of advice.

Jennifer Gillette
I think it's huge. I have another one here for you, Dr. Wang, from one of our buddies. Have you often seen cardiovascular complications from transplants? Which are the most prevalent?

Dr. Trent Wang
Yeah. That's a good question. Cardiovascular complications is such a broad term. So, I'll just give you a few examples of what are the most common. When you're undergoing the transplant itself, you're on a lot of medications, including tacrolimus or sirolimus. Tacro has this nice impact of directly increasing the blood pressure, which can also lead to stroke risk, heart attack risk, the usual blood pressure risks, and why we treat it in the first place. So, that's a direct transplant complication.

The chemotherapy from transplants sometimes affects the heart and can weaken it. Fluid treatments, medications that reduce our absorption, immune suppressants sometimes affect our absorption of other things. And when our nutrition decreases, we also have more swelling. But in addition to that, sometimes the cardiovascular components of it, such as the heart maybe not being as strong or stiffening over age, especially if you had preexisting cardiovascular issues, can contribute to that.

Over the long run, yes, chemotherapy, having a history of it, having a history of the immune suppressants and GvHD as a general, all increase your risk of cardiovascular complications, stroke, heart attack, in the long term. Many metabolic factors from medications that we use such as sirolimus can also raise those risk factors and increase your sugars as well. I mean, there are so many. And steroids are one of the biggest culprits--very, very prevalent. We have to control you blood pressure and make sure you get your cholesterol checked. And you can't break up with your primary care doctor.

Jennifer Gillette
Important note there. Thank you. Thank you, Dr. Wang. I cannot believe that we are already to the end of this presentation. But wow, what a dream team we have had here today. And I thank you, Dr. Wang, I thank you, Dr. Traeger, and I thank you, Michael, for just so much meat with

this presentation. I also want to thank our sponsors, Sanafi and Incyte. We appreciate you supporting this program.

And I want to let everyone know that this will be on our website within a couple of days as well as if you had difficulty getting the slides. That will be on our website within a couple of days as well. We will be sending you a quick survey at the end of this webinar. It just helps us for future programming and makes us aware of things we can do to maximize these calls for you. But again, I want to thank everyone for being here today. And we hope that you found this program helpful. Have a great day.

Operator
Thank you. That does conclude today's webcast. You may disconnect your line at this time, and have a wonderful day. We thank you for your participation today.