NBMT LINK
Power Panel Webinar
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Presenters
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Dr. Andy Harris, Memorial Sloan Kettering
Dr. Doris Ponce, Memorial Sloan Kettering
Dr. Alina Markova, Memorial Sloan Kettering

Q&A Participants
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Operator
Ladies and gentlemen, welcome to today's NBMT LINK Power Panel Webinar, Symptoms & Signs of Chronic Graft Versus Host Disease: Let's Learn from the Experts at a Multidisciplinary Clinic Regarding Ways You Can Better Advocate for Yourself Before Symptoms Worsen.

It's now my pleasure to turn the call over to Executive Director, Peggy Burkhard. Please go ahead, Peggy.

Peggy Burkhard
Thank you, Kevin. Welcome, everyone, and Happy New Year. Welcome to our first Power Panel. We're very excited to host this today. Thanks to Sanofi for being our sponsor. Just so everyone knows, there will be a short survey after this program, and anyone that fills it out and would like a free GVHD book, it is yours for the filling out. So we hope to hear from you. We have English and Spanish books, and you are welcome to one or the other upon request. So let's get started.

Today we have with us, Dr. Andy Harris, Dr. Doris Ponce and Dr. Alina Markova of Memorial Sloan Kettering Cancer Center. Excuse me. Just a few things to note before I introduce our panel. Please be sure to check out our website to learn more about our available resources, including books and programs. And as well, like us on Facebook and you'll receive daily inspiration thanks to Jen Gillette, our LMSW on staff. Speaking of Jen, should you want a mentor or one-on-one support, Jen is available, and you can reach out to her at the email address on the slides.

As I mentioned, we are offering a free book to all participants, and if you fill out the survey, you will be able to grab that. We're very excited to have that book in Spanish. So let's get on with it.

Just so everyone knows there, there is a show captions button on the bottom of the screen for those that would like closed captioning as an option.

So today, everyone, this dynamic team will educate viewers regarding ways to better detect early symptoms and signs of chronic GVHD. These experts will show us how to incorporate sub-specialist care into chronic GVHD management, resulting in empowerment and better outcomes. After the formal presentations, there will be time for questions from attendance.

So a quick rundown of the program. Dr. Andy Harris will address symptoms and signs of chronic GVHD, educating patients on what to look for in order to empower them to detect things as early as possible and then contact your doctor for evaluation. Dr. Doris Ponce will tell us more about their successful multidisciplinary clinic model and what those who don't have access to a similar clinic can do to advocate for incorporating subspecialist care into their GVHD management. Then we have Dr. Alina Markova, a dermatologist, who will focus on the role of a sub specialist in chronic GVHD, care given to a myriad of systems that can be affected by GVHD.

Each speaker will present for about 12 to 15 minutes, and then again, we'll have questions at the end. First up, before I get to Dr. Andy Harris, who is a dear friend of the LINK, I do want to mention the medical disclosure as seen on the screen. And then I'll move on to introducing Andy, who is a member of the MSK Kids' Transplant and Cellular Therapies program at Memorial Sloan Kettering Cancer Center in New York City.

He serves as the Director of the Pediatric Transplant and Cellular Therapies Fellowship, Associate Director for the combined Memorial Sloan Kettering Weil Cornell Pediatric Hematology Oncology Fellowship, and is a director of their Pediatric Multidisciplinary Graft Versus Host Disease Clinic. Phew. Dr. Harris is an internationally recognized expert and performs clinical research in graft versus host disease. Dr. Harris is also a leukemia survivor, who had an allergenic bone marrow transplant in his late teens.

Welcome, Dr. Harris, and thank you so much for being here today and helping me coordinate this effort.

Andy Harris
Thanks, Peggy. So Peggy asked me to talk a bit about the signs and symptoms of chronic graft versus host disease, things that you can be looking for at home so that way you can try to identify them early, because early detection is really key to maximizing the response to treatments and minimizing long-standing symptoms that can occur from chronic graft versus host disease. So I'm not going to go over this slide in great detail, aside from saying that chronic graft versus host disease can affect almost every single organ and system in the body, and so it's really important to be in tune with your body and pay attention to changes that happen in your body after your transplant and bring these up to your doctors whenever you see them.

I am going to go through some of the more common manifestations of chronic graft versus host disease over this next few slides to help you identify things that may be related to chronic graft versus host disease. The reason that it's important to detect chronic graft versus host disease early is that it can involve fibrosis or scarring, and these changes may take either months or years to resolve, and some of these changes may be permanent and irreversible. So therefore, treating chronic graft versus host disease as early as possible will limit or prevent some of these long-standing changes, to minimize long standing injury, disability and changes to quality of life associated with chronic graft versus host disease.

So I'm going to go through most of the major organ systems that we think about when we talk about chronic graft versus host disease and what to look out for. And I'm going to start with the skin, because it is the most commonly involved organ with chronic graft versus host disease. The most common manifestations of chronic graft versus host disease of the skin are new rashes, but these rashes can look like many different things. It can be a red rash or dry patches on your skin, or silver or scaly patches on your skin. It can also involve pigment changes, meaning areas of lightening of the skin that can be referred to as depigmentation or vitiligo, or darkened areas of the skin, which we refer to as hyperpigmentation. This can also involve thickening or tightening of the skin, which we refer to as sclerodermatous changes, and these can be very challenging to manage, because this is some of that scarring and fibrosis that we worry about with chronic graft versus host disease.

Chronic graft versus host disease can also affect the nails and the hair and lead to brittle nails, nail changes or nail ridging, or hair loss with or without scarring of the scalp or premature graying of the hair. So if you notice any of these changes in your skin, please contact your treating transplant physician very early to discuss these and then request additional evaluation. These next few slides, I'm going to show some pictures of some of the changes in the skin that can be seen. These tend to be some of the more severe manifestations of these different types of chronic graft versus host disease that can involve the skin.

And the one on the left here is what we call poikiloderma, and this can have areas of darkening of the skin, hyperpigmentation. It can have this telangiectasia and erythema, which is redness with what looked to be very superficial, small blood vessels. And it can lead to thinning of the skin, which is called atrophy, or lightning of the skin, which we call depigmentation. On the right is a manifestation of chronic graft versus host disease with the skin that we call morphia, where you have this darkened border around these well circumscribed areas of skin, where you often will have scarring and lightning of the skin inside these sharp borders here. And this also is a fibrotic manifestation that can take a long time to reverse if allowed to persist for a long period of time before starting therapy.

Lichen sclerosus, which you can see on the left here, is another one of the diagnostic features of chronic graft versus host disease of the skin. And here you can see superficial brittleness of the skin. What they refer to this as, is cigarette paper skin, which I think we need a new name, because I don't think most people know what cigarette paper looks like anymore, but we

haven't come up with a new term for that just yet. And then the picture on the right, there's Lichen planus. This is an area of silver scale with surrounding erythema. This can be a raised patch, or can be flat, and sometimes can feel stiff to the touch.

The more classic sclerodermatous changes that we worry about can lead to skin dimpling in areas where you wouldn't expect to see dimpling of the skin. So in these first two pictures on the left, you see some superficial sclerosis of the skin, where you have dimpling on the arm where you wouldn't expect to see that dimpling otherwise, and on the abdomen of this gentleman, in areas where gravity would not lead to dimpling otherwise. When the sclerosis gets a little bit more severe, it can lead to what we call high-bound sclerosis, where you cannot pinch the skin away from the underlying soft tissues and bones. And this is a little bit more severe scleroderma. And this can happen first at presentation, or it can be an evolution of untreated sclerosis of the skin.

Moving on to the eyes and the mouth, which also can be frequently involved with chronic graft versus host disease. With the eyes, you can have dry eyes or sensitivity to the light, which is called photophobia. You could have eyes that feel gritty or like a sensation of foreign body or sand in your eyes when you close your eyes. It can lead to eye pain and redness or swelling of the eyes or the areas around the eyes. Chronic graft versus host disease that involves the mouth can lead to white or lacy appearance inside of the mouth. These are what we call ligand noise changes in the mouth, and I'll show a picture of this on the next slide.

If there's significant fibrosis or scaring, this can lead to the decreased ability to open the mouth wide, and can also lead to a dry mouth. Other things that we can see with chronic graft versus host disease of the mouth are bumps that we can call mucoceles. These may be painful or painless, and sometimes we can see blisters or sores in the mouth that we refer to as ulcers. We can also see generalized redness and inflammation inside the mouth and oral sensitivity, which is pain that can be associated with different foods, such as things that are minty, like toothpaste or minty foods, spicy foods, acidic foods or with citrus.

Here are a couple pictures of graft versus host disease involving the mouth. On the left, you can see areas of redness, which is inflammation. You see this blister on the roof of the mouth here. And you can see some alterations of the mouth. The picture on the right shows more of these more classic lichenoid changes, where you see these white bands along the mucosa of the cheeks.

The lungs are one of the organs that we worry about getting involved with chronic grapplers associates, because this is one that's more associated with poor outcomes in patients. And some of the more early signs that we see with lung GVHD is development of a chronic cough or new or worsening shortness of breath. This can lead to decreased ability to exercise, and in our younger patients who don't routinely exercise, it may lead to limitations in play when having active play time with their peers, such as in recess. This can lead to difficulty walking or climbing

stairs. And it's important to determine whether this is due to limitations because of muscle weakness or because of inability to catch your breath, which is more associated with the lungs.

One thing your doctor should be doing periodically after your transplant is getting breathing tests, or this pulmonary function testing that we do for patients, everybody gets this before transplant, and it should be done periodically after transplant to look for early signs of chronic graft versus host disease of the lungs, to try to catch it before you have active symptoms. These breathing tests cannot be performed in young children because they're not able to do these difficult breathing maneuvers. And so we're looking at some new tests for screening in younger children that aren't able to perform these PFTs, and so there's research being performed in that area.

As far as the digestive tract, we can see difficulty with swallowing or food getting stuck when swallowing, when chronic graft versus host disease affects the esophagus. When it affects the lower GI tract, it can lead to loss of appetite, nausea, vomiting, or even further down, can lead to diarrhea. Additionally, this can lead to unintentional weight loss for patients as well. As far as muscle and joint involvement of chronic graft versus host disease, this can lead to decreased mobility of the joints, so inability to lift the arms at the shoulders or straighten or bend the elbows, make a fully tight fist or fully extend the fingers, like when putting your hands together to pray, tightness of the wrists or ankle stiffness. It can also lead to joint pain, muscle pain, or swelling of the extremities as well.

On this slide here, you'll look at maneuvers that doctors often will have patients do to look for any involvement of the joints with chronic graft versus host disease. And here you see a patient in the top row fully raising their arms up above their head, showing full flexibility and mobility of the shoulders. And here, you have a patient that's showing full ability to straighten the arms at the elbow. This next one is what we call the [inaudible], where we're able to put the hands and fingers together flat and bring our elbows out to the side.

When we look at ankle mobility, we look at how high we can bring the toes up and bring the foot up towards the knee, and patients that have restricted mobility aren't able to fully bring their ankle up like this. And so this will be scored by your doctor when they're assessing your joints and muscles for involvement of chronic graft versus host disease. On this, you see a patient that has some limited mobility in the fingers and wrists in the picture on the left, and inability to fully raise their arms above their head on the right because of involvement of the shoulders. And so when we see these, these are concerning for involvement of chronic graft versus host disease.

Chronic graft versus host disease can also involve the genitals. And when involving the vagina, this can lead to narrowing or [inaudible] of the vagina. It can lead to sores or ulcers in the vagina and on the vaginal mucosa. This can lead to pain with sex, which is called dyspareunia, and also the generalized redness or inflammation of the mucosa of the vagina. When involving the penis, it can lead to tightening or thickening of the skin, including the foreskin. It can lead to

scarring or narrowing of the urethra, which is the opening at the tip of the penis. It can lead to redness or irritation, and because of some of this irritation, it may lead to pain or difficulty with urinating for our male patients.

So the big picture is this chronic graft versus host disease can affect almost any part of your body. So if you notice anything that looks or feels different after your transplant, please feel empowered to contact your transplant team early to discuss this and ask to be seen for further evaluation.

So that concludes my talk, and I'll pass it back to Peggy to introduce Doris.

Peggy Burkhard
Well, thank you, Dr. Harris. That was awesome. We so appreciate it. Next up, we have Dr. Doris Ponce, and I will tell you a bit about her. She is a physician scientist with a career focused on patient-oriented research. Dr. Ponce is a hematologist oncologist with adult bone marrow transplant training and holds a Master's degree in clinical trial design in oncology. Dr. Ponce serves as director of the GVHD program at Memorial Sloan Kettering and co-chair of the Center for Hematologic Malignancies Research Council. That was a mouthful. She leads the Institutional Adult Multidisciplinary GVHD Clinic, oversees the research portfolio in adult GVHD, and serves as PI on multiple institutional and national studies.

Her research is supported by multiple sources, including federal funding and industry and institutional grants. Dr. Ponce is a member of the CIB MTR Working Committee for GVHD and chair elected of the Toxicity and Supportive Care Committee for BMT CTN. Dr. Ponce participates in lectures and educational activities across Latin America, and recently chaired the GVHD symposium for the region.

Welcome, Dr. Ponce. Thank you for being with us today.

Doris Ponce
Thank you so much, Peggy, and thank you for having us. As you know, the three of us are honored to be here. So I'm going to jump into my topic. So we're going to -- what I'm going to be talking is a follow-up from Dr. Harris about what all these symptoms of graft versus host disease, why we have a graft versus host disease clinic and what to do if a patient doesn't have access to it. So coming from Dr. Harris's discussion, we know that graft versus host disease can affect many, many organs. Officially, by NIH criteria, which is the National Institute of Health that dictates what we do for assessment in graft versus host disease, we recognize there are eight organs affected, but sometimes we have atypical presentation that can go beyond that.

[Inaudible]

Operator

Dr. Ponce, this is the operator. I'm sorry to interrupt you. I'm so sorry. I just want to make I need to maximize your screen for you, Doctor, if you don't mind. So above your screen where it says display settings, would you mind clicking that for me and then go to the dual screen mode, please? Sorry to interrupt, everyone. It's just the participants cannot see correctly.

Doris Ponce
Sorry, where do I need to go?

Operator
Right above your slide, where it says display settings.

Doris Ponce
I am so sorry. Oh, display settings. Yeah.

Operator
Yep. Please click that and then click duplicate slideshow.

Doris Ponce
OK.

Operator
Thank you. Please proceed.

Doris Ponce
OK. Shall I start, or -- OK. So taking from Dr. Harris, we know that there are multiple organs affected. So we're always at the lookout for symptoms where graft versus host disease can affect. So in this side, from Dr. Lee, we know that graft versus host disease is particularly more common in affecting the skin, mouth and eyes. So those are the three organs that we will always try to be like a deep investigator, among others, but these are the one that usually start giving signs of graft versus host disease at the beginning, when it's starting to develop.

So what do we look at for patients that we think will have [inaudible] of graft versus host disease? So when they come for clinic, we make a curated list of questions, trying to address those organs, those early symptoms of graft versus host disease. We try to pick this up earlier rather than later, because, as you will learn with Dr. Markova's presentation, if we identified a patient that is earlier in the process of graft versus host disease, we can contain their symptoms easier than if there's more advanced presentation.

So in this case, we ask about -- for example, for the skin, we ask if they have any tightness, if they have any sores, they feel itchy. Those can be early manifestations. Sometimes patient could have changes in their scars, like from previous transplant, or some patient describe their skin being scaly, or changes in color, like darkening of the skin, or even having signs of vitiligo, for example.

We also can see changes in their hair, like new hair loss, or changes in the texture of the hair, like more thinning. The nails can also become fragile and different. And sometimes the patients don't even report that, but it's something to look at for initial signs. And then eyes are quite common, and they can start reporting this as an allergy sensation. The patient will feel dry, gritty, or actually the opposite. They could feel very teary, like they're crying all the time. And that can all be a sign that there is irritation in the layers of the eyes. And sometimes it's not even reported by the patient. They could buy artificial tears over the counter and not even talk about it when they come to a visit.

Other signs or questions that we try to focus is for musculoskeletal, so some patients that have joint pain or difficulty doing exercises or feeling that they're swelling in their ankles or other organs. Also for vaginal symptoms and difficulty for sexual intercourse can be common. And then another organ that we look at is for the lungs, where patients can report having shortness of breath or coughing.

Also, it's not included here, but as Dr. Harris mentioned, a patient could have GI symptoms, so diarrhea, difficulty swallowing, oral symptoms as well, like sores, issues with spicy food or brushing their teeth with a regular toothpaste and toothbrush can be a new report as well. So those are things that we look at very closely. So in conclusion, if the patient has any symptoms coming up that are new or that you might be thinking could be attributable to allergies to a food [inaudible] it's always important to bring it up to the physician who's seeing the patient, because these could be signs of graft versus host disease that we don't want to ignore.

So when they come to our clinic, these are things that we look at. Dr. Harris showed a picture of a patient that have very limited mobility. So some would think that we're looking at how the patient moves, and we provide this range of motion photo guide for patients to know what they need to do, but basically, we're looking if they can move their shoulders, they can move their elbows, they can move their wrists. And also, we look for the ankles as well. Dr. Markova helped to develop these photos, and they're very helpful. We also have a version for children, so adults and children can be affected as well.

So we talk about the evaluation. So what do we do? So we do a detailed history as far as the graft versus host disease assessment. We do a physical exam where we look for that range in motion of how they move, but we also take a look at what their skin texture is, what changes they have, how their mouth is. And we basically try to focus on all these organs, looking for early signs of graft versus host disease. And then we do some blood work that can also help us to tell us if there's any [inaudible]. For example, if there's abnormalities in the liver function test can also be telling us some liver involvement, or if there are protein in the urine, can talk about some kidney issues that sometimes can be associated in graft versus host disease. So with the laboratory results, that give us some clues as well, if there's any systemic involvement.

So what is a graft versus host disease clinic, multidisciplinary clinic? So how do we build it? So the graft versus host disease clinic is basically a team of doctors that work together to take care of patients with graft versus host disease. Patients can be seen in the early phases of graft versus host disease when they're newly diagnosed, mild symptoms, or it could be seen with more advanced graft versus host disease. Many of the patients that come to our clinic, the majority have moderate or severe symptoms, which is not ideal, because you want to, again, to start early in the game.

So as we spoke about all the affection [ph] that we can see, like graft versus host disease can affect many organs. So in light of that, we built a team created in what the needs of our patients are. So as you know, we spoke about, the most common organs being affected is the mouth and the skin and the eyes. So we have a team that is composed with these specialists. So we have Dr. Markova, who is a dermatologist. We also have dentist staff. We have an ophthalmologist, an eye doctor. We have a gynecologist for female patients. But we also have other team members, like for example, we have a dietitian, who is important because these patients need nutritional support, and this is a question that comes up very often.

We also work very closely with our physiatrist who sees all our patients in clinic, and they provide a rehabilitation plan for patients who are very much in need, not only caused by graft versus host disease, but can also be caused by the treatment that we use, such as steroids. And we also bring into our clinic, as needed, we have social worker, physical therapist, research team, nursing students, just to help our patients through the journey while having graft versus host disease and how we can help them in their clinic visit. So this is why we call it multi-disciplinary. So we have multiple specialties.

What we do is that everyone sees the patient, and we see them in tandem, so one clinician sees the patient to the other, so we can envision that it's a long clinic day. So this is just an example. Let's say the patient comes to clinic. It could be in person, or it could be a telemedicine visit. And our nurses, who have been trained in graft versus host disease, or nurse practitioner, will approach the patient, and we'll do all these detailed questions that are very [inaudible] focused, like when we started -- when I started talking about, are your eyes OK, your skin is itchy. So all these questions are curated for graft versus host disease, looking for early signs.

We implement that with our nurses or nurse practitioner to approach the patient first, and that gives us the initial clues of where we will need to focus our evaluation. Then patients go through some testing that we plan for them, especially the first time we're seeing them, and then they're seen by the team of the graft versus host disease clinic. They see them all for beginning, and then we curate their assessment depending on what their needs are and what is the diagnosis.

Let's say, if the patient doesn't have any pulmonary symptoms and their testing for the lungs is completely normal, then they don't need to see the pulmonologist when they come to clinic for follow-up. On the other hand, if the patient had, let's say, additional issues that needs to be

addressed by -- especially, for example, kidney issues, we will refer the patient to a specialist, not necessarily in our staff, seeing the patient at the time visit. But basically, the structure that we have is that we all meet in one place and we all see the patient in that same visit.

There are other clinic structure nationwide, where you might see one patient -- one clinic with one physician, one specialty, one day, and then you see in another day or the same day in different places. But the model that we built is that everyone in one place. And then patient follow-up, we do quality survey assessment and we do the [inaudible] just to learn from our patient and how things are moving forward.

So one of the limitations that we have found about clinic is really where you are located. So if you're not close to a center that provides you with the clinic, the amount of patients that come exponentially decreases. So the closer you are to the center that is providing the care, the more the patient comes to visit. But we had found that telemedicine visit has actually increased that amount of patients have gone to our clinic that even though they're far away. However, we believe that -- well, with COVID, we increased the access to telemedicine like from zero to 1,000, but we believe a hybrid model is ideal, because you still want to have that in-person interaction every so on, because some of the assessment that we do, you do need -- like, you want to feel the skin, you want to measure the strength. There are things that are limited through telemedicine, but we can still provide care and guidance.

And in our model, what we like to implement, is that we can provide support to their local community. So if they come to clinic and they are seen, they can then go back to their local doctor and have continuity of care, and we can provide guidance. So not necessarily they need to teleport to, in our case, to New York and stay here. They can have an initial visit with us, and then we can provide guidance on what to do later.

So saying that, we did a quality of life assessment in our patients in clinic, and we found that patients had a lot of symptoms when they came to clinic. Some had pains. You can see here, this is the before, and -- the top of the figure is the before and then we did a follow-up survey. And since then, were tired, they didn't enjoy life that much, or difficulty sleeping. And we found that as they start treatment and they see us, some of these symptoms start getting better, but the thing that was significantly improved is the distress [ph] level. So we interpret that as, does the patient have anxiety just related of being here? And that by coming to a team that can address and take care of them, that actually, that distress level seems to be decreased among our patients, so we felt very encouraged when we saw those results.

So now I want to turn my conversation a little bit about a real case and what -- so when you don't have access to a graft versus host disease clinic, how can you advocate for yourself? And I want to give an example of how you should not advocate, like what is the things that might not go so well, so that can give you guidance of what then will be the ideal way to do it. So we have this patient who had a transplant and -- a 68-year-old. And this patient relocated to Florida, as many of our patients do, and this patient started to have changes in their skin. So the skin

started to become dark, especially in [inaudible] areas, and started to have limitations to mobility, especially with the hip, the legs, the arms, the fingers, to the point that even dressing was a chore, to put on the belt, put on the shoes, tie the shoes.

So this this patient went to a sports medicine physician, and the sports medicine physician diagnosed him with degenerate joint disease, bilateral hip. And he was scheduled for bilateral hip replacement surgery. And at that time, the patient called my clinic, called my office, saying, you know, I want to let you know that I'm being scheduled for double hip replacement surgery and I want to know if I need to take any precautions for the surgery and to let you know. And at that time, we asked the patient to come to our clinic for assessment. And ended up that this patient didn't need [ph] a surgery, what the patient had was graft versus host disease that was limiting their range of motion.

So the sport medicine physician didn't have the background or expertise in graft versus host disease. And after talking later, this was the first patient they were seeing with graft versus host disease. So it was not on their radar, and the radar was that with generative [ph] joint disease, this is more common in the general population, and therefore surgery was indicated. So here the question is, this patient has graft versus host disease symptoms, and obviously it did, like with the skin changes, the limitation for range of motion, multiple joints, and if he had done something different.

So in this case, we recommended coming to clinic, and we actually started treating for graft versus host disease, and then the patient started to regain mobility, including their hips. And obviously, the surgery was not needed. So I wanted to bring this as an example, because it did happen to one of our patients. But also, when you're looking to advocate to yourself, you want to look for someone that has some contact or is open to evaluate patients with a background of graft versus host disease.

So this was the patient, and we can see some of these changes, limitation of range of motion that the patient had. And for us, when they came to our clinic, was very obvious what was going on. But not for all the other specialties, it is. So what we recommend is that all these symptoms of graft versus host disease should be monitored closely. What you can do to yourself is to learn what those symptoms are like. For example, the questions that we went over and if something is odd or missed or new, it should be reported [inaudible] should be reported. So if you're still connected to your BMT specialist, that could be a point of care for an update.

If there is no whatsoever, I think the best second person will be your PCP or your local oncologist, and then they can triage you with the necessary care. For example, for this patient, he went straight to the sport medicine physician. He didn't really centralize the care. I do think that centralizing the care, especially if you're on your status of transplant, it will be ideal. So I recommend to avoid this individualized, independent assessment, without centralized care.

And then, remember, symptoms can happen any time after transplant. It usually happens in the first year or two, but it could happen after years later. I have patients being like, I can't believe that five years have passed and they have a graft versus host disease, so it can happen several years later. So don't take this off your radar if you're already graduated year one of your transplant, because it could still happen.

So ideally, you could seek for specialists who have some kind of essential transplant experience, and your BMT clinician can refer you to some of those. There are websites that can have a list of providers, like BMT InfoNet has a list of providers that specifically are have BMT expertise, other specialties, and also lists of multi-disciplinary clinic that maybe will be close to your neighborhood or to the city where you live. And also, BMT [inaudible] can provide guidance as well for this.

We, for example, have a website. I'll just put it here, and it does give you some of the teaching information about graft versus host disease. So access to info is really critical. I just put this as an example, but there are many, many that you could access. And for example, here, we talk about the clinic and how you can access care with us, but there are other websites as well. And I think, ideally, going close to where you live, or to your primary BMT provider will be ideal.

All right. Thank you so much.

Peggy Burkhard
Oh, thank you so much, Dr. Ponte. That was fantastic. And last, but certainly not least, we have Dr. Alina Markova with us. At Memorial Sloan Kettering Cancer Center, Dr. Markova is the vice chair for quality in the Department of Medicine, and section head of General and Onco-dermatology. Her clinical practice focuses on care of patients with cutaneous graft versus host disease and side effects from cancer or cancer therapy.

She co directs the Adult and Pediatric Multidisciplinary Graft Versus Host Disease Clinic. Her research advances diagnosis and novel treatments for cutaneous GVHD and cancer therapy related toxicities to support continued anti-cancer care therapy and long-term survivorship. She is a principal investigator on multiple clinical trials, investigating GVHD, immunotherapy dermatologic toxicities, radiation dermatitis, breast cancer cutaneous metastases and cancer therapy-associated hair loss.

Welcome, Dr. Alina Markova. Thank you so much for being with us today.

Alina Markova
Thank you so much for having me, and it's my pleasure to co-direct the Adult and Pediatric GVHD clinics with Dr. Ponce and Dr. Harris, and I will try to move through quickly. So today, my goal is to have you understand the various ways that sub specialists may address the dermatologic symptoms of graft versus host disease, and also to briefly summarize the

pharmacologic and non-prescription treatments that are available for patients like you, with cutaneous graft versus host disease.

So when we talk about cutaneous GVHD, we really talk about not just the skin, but also the nails, the hair. And I'll also touch upon, even though this is not really part of the skin, but the mouth and the eyes briefly, just so you are aware of what treatments are available. There are two main presentations of skin GVHD, and today, we're really focusing on the chronic graft versus host disease, which typically presents after day 100 and has the specific manifestations that Dr. Harris and Dr. Ponce previously covered.

So the two main types of skin GVHD that we like to think about is the epidermal chronic graft versus host disease, which is the non-scarring type. So the one that really involves the skin and can cause these scaly rashes and discolorations and redness, but really doesn't create that bound-down or hard to pinch feeling. And in different skin types, this can present differently. It can be very extensive, and it can involve the external lips, the thighs [ph], and it can have this kind of purplish color. So that's something to note. Anytime you see any sort of skin change that is new, you should bring it to the attention of your bone marrow transplant team and dermatologist. This can involve the palms and have these papular lesions as well.

For skin GVHD, most treatments for the epidermal type where it's non-scarring, not tight, topical treatments can actually work quite effectively for localized involvement and for symptom control. So topical steroids, topical calcineurin inhibitors such as pimecrolimus and tacrolimus can be helpful, and these are readily available via prescription from your dermatologist or bone marrow transplant physician. There's a study previously also with topical ruxolitinib cream that showed some efficacy as well.

When the rash is more extensive, that's when we really can consider treatments like phototherapy. There's this type of phototherapy that's called Narrowband UVB phototherapy, and it's used primarily for eczema and psoriasis. And this can be effective in GVHD as well, and this is usually organized by a local -- or dermatologist. For the topicals, one thing just to be aware of is, when you receive a topical, it can come in different forms. So if you're getting a steroid, it can come as an ointment, which is very greasy, or an oil which is -- also can be greasy or cream. And these have generally no alcohol or very little alcohol. They're water and oil based. And so these are when there's broken skin, these are what's best to receive and use on the skin.

However, if you have a large body surface area or a hairy area that you're trying to apply to, sometimes the creams are just too sticky, and that's when we really like to prescribe things that have alcohol, like foams, gel, sprays or solutions. And these are good for the scalp, for any hair-bearing areas, and really when you have intact skin, so that means no open areas. If you have open areas and you apply one of these vehicles that has alcohol in it, it will burn. It's not a side effect. It's just something that happens with alcohol onto any broken skin. So when you're

receiving a treatment, if it's not working for you or it's hard to apply, give that feedback back to your prescribing physician, and they can modify it to be something that's easier to apply.

Phototherapy, you can find it through your local dermatologist. The American Academy of Dermatology also has a Find a Dermatologist portal, and you can actually select phototherapy, and they can show you which dermatologists administer phototherapy near you. Moving on to sclerotic, which is a scarring type of GVHD, so the one that's harder to pinch. And this is what has already been reviewed by Dr. Harris and Dr. Ponce. And one thing to note is it can appear in areas of prior trauma, so even the waistband of underwear or the bra strap or a prior surgery. So if you see any new changes to old scars or anything around frequent trauma areas, definitely bring that to the attention of your physician, so that they can evaluate and diagnose you as early as possible.

When the skin is very tight, it can actually lead to limitations and range of motion, similarly as just primary GVHD of the joints. So sometimes we do have to treat the skin in order to improve the range of motion. And we do follow the range of motion with the [inaudible] that Dr. Harris previously presented. Again, when the skin is very tight and there's poor skin integrity, this can lead to chronic wounds. So it's not uncommon to see wounds, especially in the legs and feet and in extensive graft versus host disease, in other parts of the body.

When we treat topical -- when we talk about topical treatments for skin GVHD that's scarring, most topicals are minimally effective. We primarily use them for symptom control, so if there's itch or scaliness or dryness. But as far as the treating of the actual scarring GVHD, it's quite deep in the skin, usually even below the skin, like in the fat, and so the creams don't really penetrate. So we generally do not use topicals unless there's a symptom to be managed. And we, of course, incorporate wound care if there are wounds.

Whenever a patient comes in with sclerotic or scarring skin GVHD, that's when we really partner with our BMT physician colleagues to start a systemic treatment for these patients. There is some evidence for a different type of phototherapy called UVA1. It's only available at select sites across the country, but it can penetrate deep enough to get some of the scarring GVHD treated and improved.

Moving on to other signs and symptoms, so oral chronic graft versus host disease, this has already been covered, but there are ways we can manage this, and it is a common symptom in our chronic graft versus host disease patients. So topical therapies for these patients, from topical steroids to topical injections and topical cyclosporine or topical tacrolimus have been used as well. We also incorporate pain control, so we add lidocaine treatments that can be switched around, even sometimes oral pills that can help with the pain. So definitely, if you're having pain with your oral GVHD, bring it to the attention of your team, so they can give you something for the pain.

There are also liquid band aids that can be prescribed. Some of the brands are MuGard or Gelclair. They may be covered by insurance, but not always, and they can kind of coat your sores so that you are able to eat. There are other -- GVHD can also be in the mouth, can be accompanied by dry mouth. And there are over the counter options for dry mouth that can stimulate saliva and also that can just provide a saliva substitute listed here. And then there are prescription therapies such as cevimeline and pilocarpine. And these are treatments that, again, ask your team if you want something topical that's over the counter, that's something you can look at yourself, but you can always confirm with your team if that's an appropriate treatment for you. And then you can always ask if there's something more that can be done by mouth with a pill.

And cevimeline is used primarily in patients with this autoimmune dry mouth condition called Sjogren's. It's established to increase the saliva flow, and it's generally well-tolerated outside of some headaches and sweating. And pilocarpine is the alternative, but it's more poorly tolerated due to the severe sweating and stomach cramps that patients can get.

These are the xylitol [inaudible]. These are over the counter. These are little tabs that can be applied to the gums, and they stimulate saliva. These are great overnight if you wake up with dry mouth. And moving on to another area of GVHD, so the genital area. This can also be treated. So again, just as Dr. Harris mentioned, if there are changes in the genital area, please see an expert to evaluate whether it's the penile area or the vaginal area, and then high-potency topical steroids are oftentimes incorporated and then getting connected with a gynecologist or a urologist for additional management.

Itch is another side effect that is commonly seen. Just inform your team. There are so many things that can be done for it, from topicals to orals to injections. So another common side effect in GVHD. Nail changes can be mild, with some flaking and splitting, to more severe with complete loss of the nail. The two main things to talk to your team about with nail changes, is really ruling out a fungal infection and ruling out nutritional deficiencies. So that's sometimes checking some vitamin panels to make sure that they're not contributing to the nail changes.

We do treat nail changes, although they are very refractory, but things like supplements, like over the counter biotin, that's a pill, high-potency topical steroids and nail lacquers, such as harden the nails that are readily available, can improve some of the symptoms with the nail changes. When the nails are scarring over, really, systemic therapy is required to significantly improve them, although localized steroid injections can also be helpful.

And in the last minute or so, I just want to emphasize that sub specialists can assist with non-GVHD skin concerns as well. So always bring to the attention of your dermatologist. How do you apply the various creams and ointment, so medicated cream always goes first, then any sort of moisturizer, then a sunscreen, and then makeup. Makeup is last. Moisturizing, we generally recommend using things that you can scoop, like a cream or an ointment, not a pump bottle. The pump bottles tend to have alcohol or not as moisturizing.

We recommend mineral sunblock over chemical sunblock. Even though they're thicker, they generally are a better choice for sensitive skin. We talked about just generally being sun smart, not completely avoiding the sun, because we still want you to enjoy your post-transplant life, but just being smart, wearing a hat, UPF protective clothing and sunblock. Using makeup, we recommend choosing fragrance-free products and introducing them every few days, and replacing your products frequently, every few months to every year, depending on the type of product, to make sure that you're not carrying bacteria in your products.

Hair Loss is another issue after transplant that patients frequently have. It's very common just after the chemotherapy, but it can persist beyond that and then recur with the GVHD. It can be scarring or non-scarring, and there are various treatment options available, so from topical Rogaine over the counter to oral minoxidil and topical steroids and antifungal. So really important, again, to reach out to your dermatologists for additional guidance, and we recommend just gentle hair care, but still using a shampoo and conditioner for GVHD.

There are products that do improve the regrowth of hair, both oral and topical. Minoxidil is just Rogaine, and so that has been readily used. If a patient does not want to use a medication, these are actually pigmented concealers, little powders you can put on the hairs that can obscure the thinning. So that's another option. And hair transplant is available once the GVHD is fully burned out.

So in summary, chronic GVHD can affect the skin, hair or nails. There are many treatments available that improve quality of life for patients. Notify your care team if you develop any signs or symptoms of skin, hair or nail GVHD. And in the age of telehealth, always document any new rashes with photos. We love photos. Thank you so much.

Peggy Burkhard
Well, thank you so much, Dr. Markova. I'm sorry if you felt rushed. You did such a fantastic job. Thank you. Thank you. You covered a lot, and you did it just so well done, all of you. We are so lucky to have these three with us today. And at this time, I would like to open things up to questions. My friend Dr. Harris is going to help me lead the questions. Go ahead.

Operator
In the meantime, I just want to let everyone know, if you'd like to ask a question today, you could ask a question verbally by using the raise your hand function, or you could type your question into the Q&A pod located at the bottom of your screen. We do have a question verbally. I'm going to make your line live, and I'm just going to refer to you by your first and last name. If you are a physician, and I refer to you not by doctor, I do apologize. So the first is from Robert Mendez, and your line is now live.

Please unmute your screen, Robert.

Robert Mendez
Yes, I want to thank everyone for the wonderful presentation. Most of my questions were covered. I do have one question, and that is -- just to give you a little background, I'm 28 months out of my transplant now. I was hospitalized three times in the first 100 days, and one time since then. However, it seems to me that a lot of this is all tied to the immune system, most of these symptoms that were mentioned here and which I've suffered probably half of them. I was just curious why nothing is focused or brought up or mentioned about the immune system and the correlation with a lot of these symptoms?

Andy Harris
Well, I can take this one. So yeah, so we think that all graft versus host disease, both acute and chronic, are caused by the immune system. We think this is, the immune system that comes as part of the bone marrow transplant that's in the setting of cancer, used to help fight the cancer, turning on the healthy tissues of the body. So most of the treatments that we use for both acute and chronic GVHD are designed to interface with the immune system, either weaken it or to modulate it and retrain it in a way that's going to stop that immune attack.

So when we start many of the different therapies that are available for chronic graft versus host disease or acute graft versus host disease, we have to be aware of what the level of immunosuppression is that comes with that therapy, and what risks there are for infections. And so that's something that should be at the forefront of the mind of any doctor that's prescribing medications to treat chronic graft versus host disease, is being aware of how that impacts the immune system and risk for infections and the potential effect in fighting off their cancer.

Operator
Thank you, Doctor. We do have another verbal question. Mr. Mendez, did you have a follow-up? Your line is now live.

Robert Mendez
Yes, I have a follow-up question. Dr. Ponce mentioned a timeline. I'm just curious, again, having been out of the transplant now for 28 months, is there any chance of the grass versus host disease diminishing over time, or is it just something that pops up and could pop up 10 years after? That's my question.

Doris Ponce
OK. Great question. So there is a sensitive period of time, which is when immune suppression is being decreased gradually. That is particularly a point where we could see some graft versus host disease resurgence, even if it didn't have it before. And then after stopping immune suppression, there could be a timeline of a couple months, of usually three to six months where we could see some graft versus host disease activity. After that, so after two years, having graft versus host disease exponentially. But if there is what we can [inaudible], let's say you have some type of infection, had an old burn in your skin, or something that can trigger some

inflammatory activity, sometimes you can see some graft versus host disease activity coming afterwards. Let's say kind of really bad bronchitis, and then your lungs start getting -- like they don't heal well, we could start seeing that.

So usually, it's the first year and year two where we see the most. Some patients that linger after that, it could be [inaudible] or having an insult [ph]. And usually after year five through year seven, the chance of having graft versus host disease, if you didn't have it, or if it's all gone, is extremely unlikely.

Operator
Thank you, Doctor. We have a -- next question is coming from Keith Holman. Your line is now live. And Keith, you can unmute your line.

Keith Holman
OK. Hi. I don't know if it's possible for Dr. Ponce to pull up her first slide, which was a bar graph, but even if she can't -- and I apologize if I missed this, but can she tell us what is the difference between the blue bars and the gray bars?

Doris Ponce
Yes. So this is an old slide. The blue and the gray bars basically is the type of donor, or how you -- sorry, not type of donor, how the stem cells were collected from. So the cells can be collected from what we call peripheral blood, which means those donors donated through their veins or directly through bone marrow. Historically, patients have been selected [ph], donor who had collected through peripheral blood. Those patients have higher risk of chronic graft versus host disease. However, this brings us the point that now that we are doing transplant using newer drugs for pre [inaudible] graft versus host disease, including this medication called cyclophosphamide, it has decreased that gap of differences between the two, and we have seen that graft versus host disease has decreased even in patients who get the donor samples from peripheral blood.

So again, it's a figure that reflects the differences between getting cells directly from the bone marrow versus peripheral blood. There is inherently increased risk with peripheral blood, but with the newer platforms, that incidence is decreasing.

Operator
Our next question is coming from Johanna Mayer. Your line is now live. Ms. Mayer, please unmute your line.

Johanna Mayer
OK. I'm wondering if there are any sort of manual or kind of physical therapy or massage therapy techniques that help with fasciitis and sclerotic changes in the skin, that sort of scarring and tight fascia. Are there things that you recommend to help loosen?

Andy Harris
Thanks for the question, Johanna. So I know both Doris and I have rehab specialists that work in our GVHD clinics with us to help try to address some of these complications of chronic graft versus host disease. Certainly, stretching regimens can be of benefit, but in patients that have very tight joints, sometimes our rehab doctors will help with finding splints that will help stretch the fascia over time, that can be worn for periods of time, to help try to stretch those areas that are tight, to try to improve mobility when we have fascial involvement. I know if there is very severe sclerosis of the skin, that leads to limitations.

If the chronic GVHD is felt to be inactive, sometimes we'll even have some of our plastic surgeons do some laser therapies where they do microporation [ph] of the skin to basically try to loosen up the skin by making small areas where healthier skin can grow back in to help with increasing mobility as well. So there are some options that are available, and it's important to talk to your doctor about what options may be available there, or if they can try to find you someone with whom you can consult that can try to help work with you on some of these things.

Operator
Thank you, Doctor. Our next question is coming from Trenton Nu [ph]. Your line is now live.

Trenton Nu
Hey. Thanks for having me. Can you hear me?

Andy Harris
Yep.

Trenton Nu
Hey, I put this in the chat too. I don't know if you saw it, but I was just looking for treatment plans on GVHD of the lungs. Obviously, we're on one already. I was just wondering if there's anything new out there in addition to -- it's for my daughter. She's four years old. She's on Jakafi, and she's on the SMART therapy with Tim McCourt [ph] and all that. I'm just wondering if there's anything else to help improve that.

Andy Harris
Well, just being a pediatric patient, maybe I should take this one. So one of the big challenges that we have in pediatrics is that a lot of the drugs that are approved for chronic graft versus host disease, of which there are four that are approved for older patients, the only one that's FDA approved in younger patients is Imbruvica or Ibrutinib. However, many of us are able to get Ruxolitinib approved for our younger patients and give them ruxolitinib, or Jakafi, as your daughter is getting. There are clinical trials of the other two agents, belumosudil and axatilimab.

The belumosudil trial has just recently opened at its first centers, and I actually had the privilege of treating the first pediatric patient on the belumosudil trial worldwide, and saw them earlier today. There are, I believe, eight US centers that have this study open. There are centers around the world that are also opening the study to look at how do we most appropriately dose this medication for children? Do they have unique side effects that we have to worry about, and how are their response rates compared to older patients.

Axatilimab is another of the agents that's recently been approved for chronic graft versus host disease in adults, and they are getting ready to open a pediatric trial. This is an IV medication, and it may be worthwhile talking with your doctor about seeing if you can be referred to somebody close to home that may have either of these studies available. The only other drug of which I'm aware that people are actively studying for lung GVHD, where there have been some publications, is a medicine that has been used for prevention of chronic graft versus host disease or graft versus host disease in general, and that's a medicine called Abatacept, or batacept [ph], people will call it. And there are a couple small studies suggesting that for whatever reason, this drug may have a pretty high response rate in the lungs.

The two different studies that I'm talking about have referenced roughly a 60% to 65% response rate in pulmonary chronic graft versus host disease. But it sounds like your daughter is getting Jakafi and getting azithromycin, Singulair and then Symbicort, so they're getting very good therapy. And what is primarily used for most people, there are additional lines of therapy that may be available to her, but unfortunately, most of those will be on clinical trial given her young age, and this is something that I'm actively advocating for more and earlier inclusion of children in these clinical trials of agents for chronic graft versus host disease.

Operator
Thank you, Doctor. And thank you, everyone. That does conclude our question and answer session. I'd like to turn the floor back over to Peggy for any further or closing comments.

Peggy Burkhard
Well, thank you, everyone, for spending this time with us. This was our first Power Panel, and I'd say it was a success, thanks to the three people here, and of course, Kevin. I want to thank our sponsor, Sanofi, and I want to wish everyone a Happy New Year. And the recording will be up in a few days on our website. And don't forget to fill out your surveys if you'd like a free book from us. Thank you all and have a wonderful 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.