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Chronic Graft-Versus-Host Disease Care: Evolving Therapeutic Strategies

**Announcer:**
You're listening to *Project Oncology* on ReachMD. Here's your host, Dr. Brian McDonough.

**Dr. McDonough:**
This is *Project Oncology* on ReachMD, and I'm Dr. Brian McDonough. Joining me to discuss the evolution of care for chronic graft-versus-host disease, or cGVHD for short, is Dr. Doris Ponce. She's the Director of the Graft-Versus-Host Disease Program at Memorial Sloan Kettering Cancer Center in New York City, where she's also Co-Chair of the Center for Hematologic Malignancies Translational Research Council. Dr. Ponce, welcome to the program.

**Dr. Ponce:**
Thank you very much for the warm introduction, and it's an honor and a privilege to be here and share some of the experience and updated information that we have about chronic graft-versus-host disease treatments.

**Dr. McDonough:**
We're looking forward to it. And to start us off, Dr. Ponce, how has cGVHD traditionally been managed? And what changes in the treatment landscape are we now seeing?

**Dr. Ponce:**
Well, this is a great question to get started. So graft-versus-host disease for decades has been treated exclusively with corticosteroids as standard of care, and then we really didn't have any drugs to treat beyond failure of corticosteroids. Being a disease that can really impact quality of life, and the treatment with corticosteroids is associated with a high rate of treatment failure, short duration of response, and also side effects, it was really an unmet need to find newer treatments for patients who failed corticosteroids.

So now what has changed is that we have an approval of, now, four drugs for the treatment of patients who have failed steroids at different time points after failure that have really changed how we approach patients with chronic graft-versus-host disease, where we have increased number of therapeutic options for our patients.

**Dr. McDonough:**
And if we zero in on axatilimab for a moment, could you tell us what differentiates it from other therapies and who might benefit from it the most?

**Dr. Ponce:**
So axatilimab is a drug that was most recently approved by the FDA, and it has a very unique mechanism of action. So it does target the CSFR1 receptor, which is associated with fibrosis. So if we study the pathophysiology of chronic graft-versus-host disease, we will see that there is an inflammatory response, immune dysregulation, and then we see this fibrosis—the abnormal fibrosis. And axatilimab is targeting the pathway where fibrosis occurs, and other medications for graft-versus-host disease are targeting more the immune dysregulation and inflammatory responses. So we now have a drug that specifically targets that receptor that is involved in abnormal fibrosis.

**Dr. McDonough:**
Now, thinking about how we measure success is critical, especially as management strategies shift. With that in mind, what is the significance of pursuing partial versus complete responses, particularly when they lead to meaningful symptom control across affected

organ systems?

**Dr. Ponce:**
Yes, Brian, this is a very critical question. So traditionally, the way that we had measured treatment response is that we measure overall response. And the overall response includes complete and partial. And for graft-versus-host disease in particular, imagine a patient with severe infection fibrosis—the reversibility of those symptoms to complete reversibility is rarely achieved. In other words, the patients might have improved, but it's not completely gone.

So we do measure those patients as partial responders versus complete responders, and we will see that in most of the cases, we will have a higher dominance of partial responders over complete responses by organ. However, this might evolve with time, and with the newer drugs, we might see deeper responses moving forward.

But nonetheless, having a partial response is still very significant, as patients can report improvement in their quality of life, ability to do activities of daily living, and other things that do reflect that they are getting better. Also, partial response can also bring other improvements and other benefits such as tapering other immunosuppressant drugs, not requiring high-dose corticosteroids, and still being able to have a meaningful quality of life.

**Dr. McDonough:**
For those just tuning in, you're listening to *Project Oncology* on ReachMD. I'm Dr. Brian McDonough, and I'm speaking with Dr. Doris Ponce about how treatment for chronic graft-versus-host disease is advancing.

**Dr. McDonough:**
So Dr. Ponce, now that we've discussed the therapeutic landscape for cGVHD, let's shift gears and talk about applying this knowledge in practice. When choosing between options like ruxolitinib, belumosudil, axatilimab, and ibrutinib, how can patient-reported outcomes and preferences, like route of administration, influence decision-making?

**Dr. Ponce:**
For treatment choices, there are a few things that we need to take into account. One is that even though we have four FDA-approved drugs for the treatment of chronic graft-versus-host disease, they're not all approved for a particular landscape of treatment.

So as of right now, if you get moderate-severe graft-versus-host disease or mild chronic graft-versus-host disease of high-risk features, you will start treatment with corticosteroids as your alone treatment. And then if you have failure to corticosteroids or steroid dependency, then you will consider a second-line treatment.

For second-line treatment, there are only two drugs approved for this juncture of treatment, and those are ruxolitinib and ibrutinib. And then if you fail two agents, then we have the other two drugs approved by the FDA, which is belumosudil and axatilimab.

So as of right now, we don't treat according to organ involvement. In other words, let's say you have lung chronic graft-versus-host disease, musculoskeletal, or skin. As of right now, you don't pick the drug based on the organ, but you pick the drugs based on patient's comorbidity and based on where they are in their treatment paradigm.

The route of administration now becomes relevant. Before we had the approval of axatilimab, with the other three drugs, all these drugs were oral, but now axatilimab is IV and only IV. So it does come down to a conversation with our patients about giving an IV medication.

And there are pros and cons. For example, some patients really don't have the time to dedicate to an IV infusion that is every two weeks. Some patients travel, they are active at work, or they have other activities that really prohibit them from being consistent every two weeks.

On the other hand, I find it positive to have an IV route in options like patients who have issues with compliance or an aversion to oral medications. Patients who have difficulty swallowing, for example—like severe GI involvement—the IV route will be preferred.

So you take into account the patient's preference, time, and location to offer treatment, as well as where they are under the treatment paradigm, if they have failed a drug before, and which one you want to use next. So those factors really help to have a conversation with the patient and decide the best treatment for them.

**Dr. McDonough:**
So there's lots of variables to consider.

Let's look for a second at how the role of multidisciplinary care evolved for this disease, and what does effective collaboration across specialties look like day to day?

**Dr. Ponce:**

Yeah, I really love that question. When we started our conversation, I mentioned that graft-versus-host disease can affect multiple organs. So we have a patient that can be affected head to toe—eyes, mouth, GI tract, lungs, musculoskeletal, vaginal, tissue, liver—so there are many organs that can be affected.

And as a bone marrow transplanter, you see the patient as a whole in an integral way. But when you collaborate with other physicians, with other specialties, you really can add your tools to help your patients.

So, for example, I have a graft-versus-host disease multidisciplinary clinic where I work, and we actually have a robust group. We have a dietitian, a physiatrist, a rehabilitation doctor. We have a dermatologist on staff. We have a dentist as well, and we also have physical therapy, pulmonologists, and endocrine. So all of them really bring a lot to the table. When we see the patient, they go through all these assessments and we can get specialized care from the dermatology side and a robust physiatry rehabilitation program for them. And for example, what to eat or what not to eat. There are a lot of issues with diet.

And you can see that every specialty can add a very special angle to the overall picture that you're having. So collaborating with others interested in graft-versus-host disease can really add a significant value to patient care.

**Dr. McDonough:**
Before we wrap up our program, Dr. Ponce, do you have any final thoughts you'd like to share with our audience?

**Dr. Ponce:**
Well, some of the things that I like to touch base on is that it's important to educate our patients to be their own advocate. Many patients, after their transplant, go back to their primary oncologists—they go back home. The majority does not stay close to their base or their transplant center, so it's important that they receive education where they can recognize their own symptoms.

I have many patients that might feel that ocular graft-versus-host disease is just bad allergies, difficulty swallowing has to do with bad food that they eat, and inability to move their joint is because they're getting old. So I try to educate our patients in a way that they can really be their own advocate and they can bring this up.

And also, we try to keep our checks on our patient at certain time points after transplant so that we could help them to identify any issues ahead of time. I know that there are some platforms being built for patients to track their symptoms, and I think it could add a lot of value in bone marrow transplant, where they could identify themselves, seek help when needed, and have a strong partnership with the doctors in the community that they will be the strong frontline that will help identify those patients and treat them.

**Dr. McDonough:**
That's a great comment for us to think on as we come to the end of today's program. And I want to thank my guest, Dr. Doris Ponce, for joining me to discuss the evolving treatment landscape for chronic graft-versus-host disease. Dr. Ponce, it was great having you on the program.

**Dr. Ponce:**
Thank you so much. I really appreciate it. I'm honored to be here and to discuss all these important topics. I hope we can contribute with our conversation to support our patients and the bright physicians and medical team that take care of these patients. Thank you so much.

**Dr. McDonough:**
Thank you.

**Announcer:**
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