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Real-World Strategies for Complex cGVHD Treatment Decisions

Dr. McDonough:

Welcome to *Project Oncology* on ReachMD. I'm Dr. Brian McDonough, and joining me to share real-world cases and clinical evidence that can help guide treatment decisions in 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, thanks for being here today.

Dr. Ponce:

Well, thank you so much.

Dr. McDonough:

Well, to start us off, Dr. Ponce, can you tell us about a recent patient case from your practice where standard treatment sequencing didn't provide a clear next step in their care?

Dr. Ponce:

Sure. And I think I see this more as a group of patients rather than individual cases because it does happen with certain frequency where patients might have a mixed response. This means one organ is getting better and another organ is not, a new organ is affected by chronic graft-versus-host disease, the patient has certain toxicities that they carry from a previous line of therapy or current line of therapy, or they have certain comorbidities that make the treatment sequencing a little bit more challenging.

So there are certain scenarios where a more individualized approach is needed to assess where your patient is and what treatment they need. So, for example, I have patients diagnosed with advanced graft-versus-host disease, they start therapy with corticosteroids, and then they progress on corticosteroids or they are a steroid dependent. And at that time, they also have significant cytopenia. And let's say they have cardiac arrhythmias as a heart condition. So that really limits your next step in terms of, should you switch your patient to ruxolitinib, or would you rather go with another line of therapy—for example, ibrutinib—that is also approved for second-line therapy after steroid failure? Or can you do another treatment?

For these patients, we can sometimes adjust and start a lower dose and see if you can still achieve therapeutic response or increase the dose as you follow and monitor them slowly. So sometimes, you have to adjust how you treat your patient, which dose you use, and how you introduce new doses according to these comorbidities, toxicities, or particular circumstances that your patient might be in.

Dr. McDonough:

You presented a few cases and situations. What were the key clinical or patient-specific factors that signaled it was time to change your approach?

Dr. Ponce:

Thank you very much for that question. And I want to point out that it's important that patients still get the benefit of the treatment and not cycle out of treatment ahead of time. So for treatment response and assessment, you should allow your patient to stay on at least four months—and even four to six months—of treatment before you go on to the next one. Otherwise, you'll be cycling treatments very quickly without really achieving the full benefit from the drug. Saying that in that context, if you see in that time period a patient having worsening of chronic graft-versus-host disease or new organs being affected, you don't need to wait all that time. But if that happens, then it's time to do another treatment intervention.

Also, if you are unable to taper corticosteroids from your patient or the patients are having steroid toxicities, which are actually very

common, that is another sign where another line of therapy should be added as a steroid-sparing agent or to enhance treatment response where corticosteroids eventually could be tapered.

And we also take into account tolerability of the treatment. Sometimes, patients might be responding, but they have unbearable side effects. I recommend dose adjustment, if possible, if the patient is responding. But sometimes even with that, it is prohibitive for the patient to continue therapy. So in that case, we will consider a switch of treatment at that time.

Dr. McDonough:

So when you encounter scenarios like this, how do you think about aligning treatment choice with underlying disease biology? And where do newer mechanisms that go beyond traditional T- and B-cell targeting fit into that?

Dr. Ponce:

I think that we're talking maybe five years from now—or maybe a little bit longer—when we will be able to assess according to the chronic graft-versus-host disease phenotype what drug you should use. But as of right now at this moment, we're still using the treatment choice according to their timeline of therapy. So if you are newly diagnosed, you start with steroids. If you fail steroids, then you have two drugs available by the FDA, which are ibrutinib and ruxolitinib. If you fail that, your next choices that you have available to you are belumosudil and axatilimab. So you follow the drugs by the timeline and where they are in their diagnosis and treatment algorithm rather than the disease phenotype.

Dr. McDonough:

For those just tuning in, this is *Project Oncology* on ReachMD. I'm Dr. Brian McDonough, and I'm speaking with Dr. Doris Ponce about how real-world experience and clinical evidence come together when managing chronic graft-versus-host disease.

So, Dr. Ponce, if we take a closer look at how treatment plays out in practice, can you tell us about the role of real-world evidence in guiding your decisions for patients who don't quite match clinical trial populations?

Dr. Ponce:

Yeah, thank you. This is an important question because you are basing your conversations and therapeutic decisions on the clinical trial results and FDA indications. But sometimes, you sit in front of a patient and that patient will have been excluded from a trial. And then how do you manage that patient? What will you do differently? For example, a patient who had a second transplant, donor lymphocyte infusion, or maybe some type of disease intervention and then remission are usually excluded from these types of trials. Patients who have a coexisting infection are excluded from trials, and patients who have organ dysfunction are excluded from trials. But these are the patients who come to your clinic and need you the most.

There is real-world evidence data emerging that does help to confirm the findings from the clinical trials and guide you in terms of clinical decisions. So those observations are quite critical after a drug is approved, and we study the results from that real-world data. But also as I was mentioning, for example, a patient with severe cytopenia who you would need to start on a lower dose and then adjust will have been excluded from a trial. But this is what you encounter. So dose adjustment, how they tolerate treatment, how you monitor, and what do you do if they develop particular side effects are quite critical in how you handle your practice and patients.

Dr. McDonough:

Now, another key aspect of chronic graft-versus-host disease care is multidisciplinary collaboration. So who do you typically bring into the conversation, and how do they impact your treatment planning and final decision?

Dr. Ponce:

So maybe I have a more holistic answer because we have an established team of specialties at my institution where we offer a multidisciplinary approach to all patients with chronic graft-versus-host disease, and that team is pretty well established. And basically, the conversation is whether or not to bring our patient to that type of care. And then how often the patient should follow up. We like to offer multidisciplinary care to all patients diagnosed with chronic graft-versus-host disease at least for a baseline assessment and then for continuity of care if needed with the purpose of patients being seen in our clinic for our multispecialty input, but then they can be managed back in the community with guidance from the multispecialty approach.

There are institutions that have different approaches or community centers that have different approaches. But I do think it's important to have multidisciplinary care and not leave it up to the patient to go around to different specialties as symptoms arise. So in our clinic, for example, we offer to all of our patients to see our dermatologist as dermatologic conditions are quite common. They also see dental as oral issues are frequent. They see an ophthalmologist, pharmacist, nutritionist, and physiatrist. And we have other collaborators that are used as needed, like we have a GI specialist, hepatologist, endocrinologist for the management of side effects from corticosteroids and other drugs, and pulmonologist as well. For us, it's really important for patients to recover physically. So physiatry and physical therapy

are an important angle for clinic as well the nutritional part. The multispecialty collaboration does provide better global care to the patient. And we can offer that they could take this back to their community or back to their local doctor, and they could be managed with this hybrid component of coming to clinic and then following closely for more interval care.

Dr. McDonough:

Before we close Dr. Ponce, it's obvious you care about the patient's perspective—even how you talk about the multidisciplinary approach and about the patient and how the patient could feel more comfortable, and so you've answered this partly—but how do you incorporate their priorities like quality of life, steroid reduction, and functional outcomes into your decision-making, and how has that shaped what treatment success looks like to you?

Dr. Ponce:

More and more, we are bringing up how important it is to see the patient as a whole individual, not only from the treatment response but quality of life—getting back to work and how the patient feels are important metrics that we take into account as well as financial toxicity. So we want the patient to recover from their disease, but also to get introduced back to the community and to feel well. So the quality of life is quite critical and for them to have independence with activities of daily living and even back to work. So sometimes, we have to balance; if your patient is on a drug that's providing efficacy but let's say they're having serious side effects, maybe you can compromise that, but you can also say, 'okay, I don't want to lose my response, but let's try to minimize the dose and see if we can still continue with this efficacious response but reduce the amount of side effects.

So you balance response and tolerability, and you are prioritizing the quality of life for your patient and how they're doing. So following this principle, we try to taper medications that have the most side effects. For example, the steroid burden is quite critical for side effects. So we try to reduce this dose first if the patient is on a multi-treatment plan—for example, steroids plus another drug. So you try to reduce the drug that has the most side effects and then you continue with the others.

So this is something that can also provide you with a double benefit if your patient is still having efficacy from their other line of therapy that was added besides steroids but you are reducing the side effects from steroids. So then treatment is better tolerated overall, and patients have better quality of life.

Dr. McDonough:

As those final comments bring us to the end of today's program, I want to thank my guest, Dr. Doris Ponce, for joining me to share these insights that can help guide treatment decisions in chronic graft-versus-host disease. Dr. Ponce, it was great having you on the program.

Dr. Ponce:

Thank you so much for having me.

Dr. McDonough:

For ReachMD, I'm Dr. Brian McDonough. To access this and other episodes in our series, visit *Project Oncology* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!