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Chronic GVHD Care: Latest Therapeutic Strategies and Future Directions

**Dr. Turck:**
This is *Project Oncology* on ReachMD, and I'm Dr. Charles Turck. Here with me today to discuss new therapeutic developments for chronic graft-versus-host disease, or GVHD for short, is Dr. Daniel Couriel. He's a Professor in the Division of Hematology and Hematologic Malignancies in the Department of Internal Medicine at the University of Utah School of Medicine. Dr. Couriel, welcome to the program.

**Dr. Couriel:**
Thank you very much.

**Dr. Turck:**
So if we start with some background, Dr. Couriel, would you tell us about the current treatment options available for chronic GVHD and the challenges associated with employing them in patient care?

**Dr. Couriel:**
So, that's a great question. We do, as you know, have several more treatment options than we did a few years ago. A few years ago, we just had steroids, tacrolimus, and a number of other second-line therapies that were not FDA approved, although that does not mean they were not effective. But now we have the endorsement of the FDA in a few new agents, and the first one to be FDA approved was ibrutinib, followed by ruxolitinib, followed by belumosudil, and more recently axatilimab.

I think that there's different challenges that come up. To me, the most important one is how can we manage to bring these agents to an earlier point in our treatment to avoid the long-term toxicities of corticosteroids, right? That to me is the big question in the next several years. I think we're all very fearful about ignoring or sparing steroids. But this is chronic GVHD. This is a disease that if we plan our future clinical trials carefully, we don't necessarily have to do damage by not using corticosteroids. The second challenge to me—and there's more than two, but I'm telling you what are the ones that come to mind and that I think a lot about—is how do you sequence these treatments in the best way possible? And I don't think we have an answer to that yet. So there's a lot of personal preferences, and these personal preferences are based on experience, and a lot of times on perception and intuition. And we know, because this has been proven in our and in other fields, that intuition is frequently far from reality, right? And so we really need a more systematic way of learning how to handle the sequencing of our new therapies.

**Dr. Turck:**
Well, what can you tell us about the rationale behind and place in therapy of some of these novel treatments for chronic GVHD?

**Dr. Couriel:**
My personal experience, as I said, is my personal experience, and it does not necessarily translate the truth of each of these agents. And I think that when I tell you about it, there are different things that I have to take into account, right?

There is this generalized idea that the benefit of ibrutinib is not necessarily based on a big clinical trial, and the perception is that it's not as efficacious as it was claimed to be in the pivotal clinical trial. And I think that that may have some truth to it, but we also have to bear in mind that we usually leave ibrutinib for very late in therapy of chronic GVHD, and how late you use these modalities will have a tremendous impact on how effective they can be because as time goes by, with chronic GVHD a fibrogenic disease, the patient develops clinical manifestations that are more difficult to reverse.

So usually my go-tos as second-line are extracorporeal photopheresis, which I've used for several years. I think that the experience that

the physician has with a certain modality is something that needs to be counted into the factors that determine what agent you're going to use. I have used, since its approval, a lot of ruxolitinib with a considerable amount of success, particularly in certain organ systems. But I think that goes with pretty much any treatment modality, right? They're better for certain types of chronic GVHD than others.

And belumosudil as well; I think we all got quite a bit of experience with it, especially being the ROCK inhibitor in more fibrotic forms of chronic GVHD. Axatilimab has just been approved. I think that we're getting ready to get more experience with it. There are several combination options that need to be explored. I personally think that it's very important to treat chronic graft-versus-host disease well from the beginning. So what kind of a threshold do you have to initiate steroids? When do you call chronic GVHD steroid refractory? We know that there's a lot of different definitions and that confuses the landscape. When do you pull the trigger on second-line and eventually on third-line? All of these things are going to have an impact on how good or how bad your results are.

**Dr. Turck:**
For those just tuning in, you're listening to *Project Oncology* on ReachMD. I'm Dr. Charles Turck, and I'm speaking with Dr. Daniel Couriel about advances in care for chronic graft-versus-host disease, or GVHD.

What can you tell us about the early clinical data and recent studies involving some of these newer therapies you've been discussing?

**Dr. Couriel:**
When you look at the numbers and response rates, which is the data and outcomes we get in all these clinical trials, there's a great deal of activity to a degree that looks higher than with the agents that we've been using up until now. And so that's very encouraging. Some of the response rates are better in certain organs than others. For example, with axatilimab, it's interesting to see that you have a higher rate of response in GI tract manifestations versus others that tend to be more frequent in chronic GVHD. But it is what it is. You could also think about it from the point of view that these agents may complement each other in a combination as far as how broadly you can cover different organs.

**Dr. Turck:**
So now that we know more about the latest therapeutic developments in the pipeline and that are approved, Dr. Couriel, let's focus on their potential implications. How do you envision these therapies are going to be changing the way we treat patients with chronic GVHD?

**Dr. Couriel:**
I hope that we use a lot less steroids. And I am focusing a lot on corticosteroids because it is a part of the treatment that at some point becomes part of the disease and a very disabling part of the disease. So I think that your morbidity from chronic GVHD should decrease if we could use these agents in more creative ways and earlier on in the disease to prevent those long-term toxicities that end up blending into the syndrome of chronic GVHD. The other thing that is coming to mind, and there is data in some of these studies to support that, is that for the first time in a long time in the last several years, we started measuring quality-of-life, patient reported outcomes, etc., that we objectively documented, and these are indeed improved with the use of these therapies. So that's another factor that I take into account that's going to weigh in to the general improvement of these patients.

And then with all of this, I hope—and this is something that also has to be studied in the next 10 years—we see that we continue to improve survival outcomes in addition to quality of life outcomes in this patient population. I mean, we know that in the last 20 years we've done very well from that perspective, not only in terms of non-relapsed mortality, but also when it comes to relapse.

**Dr. Turck:**
And before we close, Dr. Couriel, do you have any final thoughts on the evolving treatment landscape or any of the other aspects of the management of chronic GVHD care?

**Dr. Couriel:**
I like the fact that I can finish with an optimistic tone. I think that in general, independent of one or the other agents, is that we have more options; we have more options that are FDA-approved, and we have more options that are more active. We're seeing that this, plus supportive care, reflect on better outcomes, survival and others. So I am extremely optimistic that we are in an improvement trend and that this is just going to get better.

**Dr. Turck:**
Well, from our discussion, it's become clear that there's a lot of potential on the horizon in the management of chronic graft-versus-host disease care. And I want to thank my guest, Dr. Daniel Couriel, for joining me to share his insights on these developments. Dr. Couriel, it was great having you on the program.

**Dr. Couriel:**

Thank you very much. Thanks for having me.

**Dr. Turck:**
For ReachMD, I'm Dr. Charles Turck. 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.