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ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

How New Therapies & Patient Characteristics cChronic GVHD Treatment Sequencing

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

Dr. Turck:
Welcome to *Project Oncology* on ReachMD. I'm Dr. Charles Turck, and joining me to discuss key considerations in treatment sequencing for patients with steroid-refractory chronic graft versus host disease, or GVHD for short, is Dr. Doris Ponce. Dr. Ponce is an Associate Professor and Director of the GVHD Program of Adult BMT at Memorial Sloan Kettering Cancer Center in New York City. Dr. Ponce, thanks for being here today.

Dr. Ponce:
Well, thank you so much for having me. I'm looking forward to our conversation to discuss more about the treatment of graft versus host disease. So thank you again.

Dr. Turck:
Well to get us started, I was wondering if you would give us an overview of the approved therapeutic options for steroid-refractory chronic GVHD?

Dr. Ponce:
This is quite a relevant question because a couple years ago, the answer would be none, and now we do have three approved FDA drugs that we will discuss. So I'm just going to mention them in the order of approval. So the first drug that was approved more recently was ibrutinib. And this was approved after a phase 2 study and is approved for children 1 year and above and adults. The second drug is ruxolitinib. This drug is approved after a phase 3 study and is for patients 12 years and older. And the third drug, belumosudil, is the most recent approved out of the three. And this drug is approved after a phase 3 study for adolescents 12 years and over and adults. So those are the three that we have.

Dr. Turck:
So based on the clinical data supporting these therapies, what should we know about how to approach treatment sequencing for our patients?

Dr. Ponce:
So this is also relevant. Since we have three drugs, how do we handle which one to use? So none of the drugs have been approved to use as an upfront therapy. So we still deal with patients receiving systemic corticosteroids when it's indicated for chronic graft versus host disease. So if a patient failed treatment and becomes refractory or is a steroid dependent, then second-line therapy is indicated at this point. So both ibrutinib and ruxolitinib have been approved for after failure of systemic corticosteroids. And then belumosudil has been approved after failure for at least two lines of therapy. So their line of approval can help us to figure out which medication can we use, also the age if it's for pediatric patients younger than 12, there's only one therapeutic option. And if it's 12 years and older, then we do have the three drugs for selection. And comorbidities or patient characteristics, which we can discuss later, can also help make decisions for treatment sequencing.

Dr. Turck:
Well I was just going to ask, how do you customize the treatment sequencing based on the severity of the patient's condition or any other patient characteristics?

Dr. Ponce:
So patient severity is quite relevant because you could have chronic graft versus host disease features that are mild versus moderate-severe. So for those who are mild, they could receive only topical therapy; for example, oral graft versus host disease, they receive dexamethasone rinses. Now if there are multiple organs that have mild features of chronic graft versus host disease or there are mild features with high-risk characteristics, such as thrombocytopenia, or if the patient had moderate-severe graft versus host disease at the time of diagnosis, then systemic treatment is indicated. So that's on one end.

And then a patient's characteristics, they would really morph into the concept that the drugs that we mentioned, each one has a particular safety profile. So you want to avoid complications that could be exacerbated by your graft versus host disease treatment. So for example, if your patient has a history of cardiac arrhythmia, uncontrolled hypertension, and bleeding, then ibrutinib will probably not be your best choice. On the other hand, if you have issues with CMV viremia, or pneumonia, then ruxolitinib might not be a good choice. And then if you have severe GI upset symptoms and issues with extreme fatigue, belumosudil might not be your choice. So in terms of treatment customization, your patient characteristics and disease severity does help to pan out how you want to customize it to your patient.

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. Doris Ponce about the medical management of and treatment sequencing in patients with steroid-refractory chronic graft versus host disease, or GVHD.

Now that we have a better understanding of the approved therapeutic options and treatment sequencing considerations for this condition, let's bring this all together. Dr. Ponce, how do we take all this information into account when selecting the best treatment option for our patients?

Dr. Ponce:
We don't have a clinical trial assessing each drug on one trial. So the data that we have is each individual drug with their clinical trial, what the results were, and then we will compare across. You can't talk about how one drug is superior to the other. I think how we take all this information is that we have one drug approved with N equals 42 in a phase 2 study, which was ibrutinib, a second drug, ruxolitinib, was approved in a larger study, which was phase 3. And then we have belumosudil that was approved in a phase 2 study. So we take this as a first step.

And the second is what are your patient characteristics? Do they have limited graft versus host disease? Is this limited with high-risk features? Does the patient have moderate or severe graft versus host disease? And where are they in their treatment? Are they newly diagnosed? Are they steroid-refractory or steroid-dependent? Or how many lines of therapy have they used? And then according to that, you could customize the treatment.

Dr. Turck:
Now we've touched on a little bit of this already, but just to reiterate, why is it so important to individualize treatment plans based on each patient's characteristics?

Dr. Ponce:
It's so important because you want to succeed with your treatment. So you want to treat your patient the right way. And you don't want to make a treatment where your adherence will be compromised. So for example, if your patient is unable to tolerate treatment and you are already expecting that they won't given their comorbidities, then treatment planning is really relevant because you will avoid putting your patient on a medication that you ultimately expect will not succeed because the patient will not be able to tolerate it or it's not the right treatment.

It's important to explain to your patient that treatment for chronic graft versus host disease is different than acute graft versus host disease. And it's important that they know that adherence is quite relevant if they want to get better and that changes in their symptoms is not expected to happen right away. So especially if a patient already had acute in the past, and now they have chronic, maybe they got better after 5 days of therapy and symptoms went away. But it's important to highlight for them that with chronic, we're not expecting to see such a rapid response. It could take longer for you to feel better, but then adhering to treatment is quite relevant. So that will be part of the conversation.

And I think the point here that is relevant is that ultimately you want to succeed. And success means symptom control, improvement, and ultimately, you want to taper the immune suppressant that has the most side effects, in this case steroids. And your other line of therapy would allow you to do this successfully.

Dr. Turck:

Dr. Ponce, as we close our discussion, are there any final takeaways you'd like to share with our audience today?

Dr. Ponce:
I think it's very relevant for us to identify patients that are in need of treatment and that waiting for things to get worse will definitely get worse. And then treating your patient from a severe status is harder than when your patient is in a mild or moderate form. So the earlier you identify your patient that has indication for systemic therapy, it should be initiated. And treatment customization is quite relevant to increase adherence and treatment success.

And as of right now we have three drugs. I think in the future, we might see even more customization according to their organ affection; we might see another drug in the pipeline becoming FDA-approved in the future. We'll look into that or maybe even combination between drugs. So right now, there is no FDA indication for such, but it's something that in the future might be happening.

So I will say as a final message, this is an exciting moment to be able to, as a clinician, offer treatment to your patient when before you had nothing. And you can improve your patient outcomes, treatment response, and their quality of life as you succeed in your treatment for chronic graft versus host disease.

Dr. Turck:
Well as those key insights bring us to the end of today's program, I want to thank my guest, Dr. Doris Ponce, for joining me to share her guidance around treatment sequencing for patients with steroid-refractory chronic graft versus host disease. Dr. Ponce, it was a pleasure having you on the program.

Dr. Ponce:
Thank you so much, Dr. Turck. I really enjoyed your questions. And thank you for the opportunity to share with the audience. Thank you.

Announcer:
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