Transcript Details
This is a transcript of a continuing medical education (CME) activity. Additional media formats for the activity and full activity details (including sponsor and supporter, disclosures, and instructions for claiming credit) are available by visiting:
https://reachmd.com/programs/cme/interdisciplinary-cross-talkputting-it-all-together-part-2/14312/

Released: 08/12/2022
Valid until: 08/12/2023
Time needed to complete: 1h 54m

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

Interdisciplinary Cross Talk—Putting It All Together (Part 2)

Announcer:
Welcome to CME on ReachMD. This episode is part of our MinuteCME curriculum.
Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements as well as the learning objectives.

Dr. Broome:
Hi, I'm Dr. Catherine Broome, Associate Professor of medicine at Georgetown university in Washington, DC. And joining me today is Dr. Carlos de Castro, Professor of Medicine at Duke university, and we're going to talk a little bit today about Paroxysmal Nocturnal Hemoglobinuria and how we manage. So Dr. De Castro, what is your philosophy on managing a naive patient who presents with PNH?

Dr. de Castro:
Well, we have to, you know, think about the context of what is this patient presenting with, is it hemolysis and the classical sort of presentation for PNH that we think of, even though the majority of patients don't present that way, if the lysis is severe enough and they become anemic and symptomatic, then yes we have to start thinking about treatment of the hemolysis and how we're going to prevent that. If the presentation is with bone marrow failure that's a whole different pathophysiology of how that comes about, so we start thinking about immunosuppressive therapy trying to raise all the blood counts, and finally, if the patient presents with a blood clot then we have to think about how are we going to treat that blood clot to get them better. And that usually involves anticoagulation. My general presentation with a naive patient when we're talking about hemolysis, is to say, okay, are you symptomatic? And then which of the compliment inhibitors that are out there are we going to choose for you? We have a choice of three, eculizumab which is a C5 inhibitor that's given intravenously, at least weekly to start out with, and then every two weeks after a four week loading period, there's ravulizumab which is a much longer acting complimented inhibitor at C5, very similar to eculizumab but it's much more convenient.

You load the patient two weeks apart and then give it every eight weeks intravenously. And finally pegcetacoplan, which was approved last year which is a C3 inhibitor and has given subcutaneously twice a week with a home infusion device that we teach the patients how to give at home. So all of these have to be considered, eculizumab and ravulizumab obviously have the longest track record in terms of treatment, we know their side effect profile, we know their long term efficacy and profile, they are very good to start out with, but some patients may not like the idea of having to come to an infusion center and may prefer something like a home treatment with pegcetacoplan given twice weekly. Pegcetacoplan is approved for all patients with PNH not just those that are suboptimal responders taking ravulizumab so we can give be given to anybody but I tend to start with the ravulizumab first it's much more convenient for the patient and we again know it's long-term side effects. And so we're comfortable with its use. Pegcetacoplan I will say is probably coming on fairly strong though in terms of being used upfront.

Dr. Broome:
Excellent, and so are there any specific clinical findings as you're then monitoring and managing your patient on a C5 inhibitor that may make you think about needing or wanting to change therapies?

Dr. de Castro:
So certainly if the patient is not responding well if they are still anemic and symptomatic from that anemia if they're needing transfusions

red cells then we have to look at the patient and say why are they not responding well? And is this suboptimal response possibly due to C3 coating of the red cells and then the extravascular hemolysis that comes with it. And if that's the case that would make me strongly want to switch them off of the C5 inhibitor saying, no this is not working well for you, you still are symptomatic from this anemia that's ongoing. And from just the symptoms of complement activation, let's try switching you to pegcetacoplan and see how you do.

Dr. Broome:
Do you notice, or do you have any thoughts about the side effect profile of the C5 inhibitor versus the C3 inhibitor? And is that something that plays into your decision?

Dr. de Castro:
They're very similar in terms of side effects, I will say that the pegcetacoplan because it's a subcutaneous infusion, we do see more infusion site reaction, so you have to be a little bit careful with that but so far patients have been able to tolerate that and learn to go through with that. And there was a little bit more diarrhea in the phase three study with the pegcetacoplan. Otherwise, the main thing we have to be aware of with all of these complement inhibitors is the risk of infection especially with encapsulated organisms such as, meningococcus and in addition with pegcetacoplan we again vaccinate against pneumococcus and HEOP influenza just to prevent those infections. The patients have to be educated about the risk of infection too so that they can be aware of the symptoms and what to watch for and know when to seek immediate attention.

Dr. Broome:
And it sounds like these patients need constant and long-term monitoring. How do you approach this long-term relationship with your patients and what kind of monitoring do you suggest for patients who are either on a therapy or maybe not needing a therapy right away but you want to continue to manage and monitor whether they do need intervention in the future?

Dr. de Castro:
Well, that's a great question. I think initially when we're first starting treatment on patients, they do have to be monitored fairly frequently to see how they're recovering, how they're responding to the medication. But once they're in a stable phase I would probably see a patient at least once every three months, maybe in some of the patients that are very very stable I'll see them once every six months but usually about once every three months. And again, I monitor their hematological parameters, I monitor their chemistries and their LDH, we look for any signs of ongoing hemolysis and really we look for how well they're feeling and doing on the medication.

Dr. Broome:
Are there end-organ toxicities either secondary to the disease or to the therapies that also need to be monitored?

Dr. de Castro:
Oh, certainly, I mean, if somebody's not on treatment and they have ongoing hemolysis, even if they're asymptomatic, I worry about the long-term effects on the kidneys, we've seen eventual renal failure developed from all the filtering of the hemosiderin, they can develop pulmonary hypertension, they can always develop clots at any point, and that's real life-threatening issue if they develop a thrombosis of some sort. So these are the things we have to think of as we go through in monitoring PNH patients and asking 'em about symptoms of those things and monitoring their chemistries.

Dr. Broome:
With our currently available C5 and C3 inhibitor therapies, do you see room for continued improvement in how we manage these patients moving forward?

Dr. de Castro:
There are many ways we can improve. There's still room for improvement in all these. We still don't have a cure for this disease short of a bone marrow transplant, which is in most cases you know, too toxic to consider for somebody who may have a hopefully normal life expectancy. So at some point we need to focus on the bone marrow failure and what causes that and how can we treat it better, because the hope would be that if we can restore normal hemolysis, the PNH clone may disappear and you won't have to worry about hemolysis. But that's still a far ways off in the future. In terms of treating the hemolysis, we certainly have a assortment of oral drugs that are on the horizon that are in clinical testing now and that would probably make their lives much, much easier more convenient to take an oral drug, better considered a shot or an IV infusion. And that will be wonderful. Hopefully those drugs will show the same promise that they're showing now, and will get FDA approved in the future.

Dr. Broome:
Excellent, well that sounds like we have a lot of really exciting things to look forward to, as we continue to care for and manage our patients PNH I'd like to thank Dr. de Castro for joining me today, and we would look forward to seeing you at our next broadcast.

Announcer:

You have been listening to CME on ReachMD. This activity is jointly provided by Global Learning Collaborative (GLC) and TotalCME, Inc. and is part of our MinuteCME curriculum.
To receive your free CME credit, or to download this activity, go to ReachMD.com/CME. Thank you for listening.