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Clinical Considerations in the Management of Myelofibrosis-Related Anemia

Announcer:
You're listening to *Project Oncology* on ReachMD, and this episode is sponsored by GSK. Here's your host, Dr. Charles Turck.

Dr. Turck:
Welcome to *Project Oncology* on ReachMD. I'm Dr. Charles Turck, and joining me to share their perspectives on the management of anemia in myelofibrosis are Dr. Raajit Rampal and Dr. John Mascarenhas. Dr. Rampal is a hematologic oncologist specializing in the treatment of leukemia and myeloproliferative diseases at the Memorial Sloan Kettering Cancer Center in New York. Dr. Rampal, welcome to the program.

Dr. Rampal:
Thanks for having me. Pleasure to be here.

Dr. Turck:
And Dr. Mascarenhas is a Professor of Medicine at the Icahn School of Medicine and Director of the Center of Excellence for Blood Cancers and Myeloid Disorders at Mount Sinai in New York. Dr. Mascarenhas, it's great to have you with us as well.

Dr. Mascarenhas:
Great to be here.

Dr. Turck:
Starting with you, Dr. Rampal, what are the current treatment modalities for myelofibrosis-related anemia?

Dr. Rampal:
Yeah, so for myelofibrosis-related anemia, there's a number of things that we can utilize. And these include drugs like ESAs, or erythropoietin-stimulating agents, and those can be used in patients who, for example, have an endogenous erythropoietin level below 250 or so. Beyond that, there are other agents that have been used historically, and those include things like danazol which is an oral drug, as well as immunomodulatory agents, and those include things like lenalidomide and thalidomide.

Dr. Turck:
Now turning to you, Dr. Mascarenhas, can you tell us about the efficacy of those treatments?

Dr. Mascarenhas:
So the efficacy of agents that we've historically used to treat myelofibrosis, whether it's ESAs, danazol, or immunomodulatory drugs, it's all collectively somewhere between 20 and 40 percent, probably safely around 30 percent, with durabilities that can range from six months to a year. And they're sometimes limited by toxicity or ultimately lack of response or loss of initial response.

Dr. Turck:
And how about their safety, Dr. Mascarenhas? What do we need to keep in mind there?

Dr. Mascarenhas:
I think each drug has a different safety profile that one should be aware of. Danazol is a synthetic male androgen. You need to be cognizant of, particularly in men, prostate hypertrophy and hirsutism in women, so follow liver function tests. I've seen patients develop pretty significant edema in some cases and have GI distress. So there's a toxicity profile – particularly to danazol – that could be quite different than thalidomide. Thalidomide's usually given as a low dose, often in combination with prednisone, so hyperglycemia and

classic thalidomide toxicities would include constipation, sedation, peripheral neuropathy, and even thrombosis. Some people would even advocate for low-dose aspirin for thromboprophylaxis, although it's not clear that that really reduces thrombotic risk in this setting. And then with lenalidomide, neutropenia and thrombocytopenia could be seen even in the setting of an improvement in hemoglobin. So different toxicity profiles for different drugs and monitoring of lab values is still important.

Dr. Turck:
For those just joining us, this is *Project Oncology* on ReachMD. I'm Dr. Charles Turck, and I'm speaking with Drs. Raajit Rampal and John Mascarenhas about the management of anemia in myelofibrosis.

Coming back to you, Dr. Rampal, what are some key considerations you keep in mind when selecting a treatment for myelofibrosis-related anemia?

Dr. Rampal:
There's a couple of things that need to be kept in mind when treating anemia in myelofibrosis. So number one, what is the patient's main problem? Is the main problem anemia, or is it anemia plus symptoms? Because using a JAK inhibitor, for example, in a patient whose principle problem is anemia probably isn't going to do them so much good as JAK inhibitors can have a number of side effects, both on target and off target. And so that's I think the first question that has to be asked: are you treating a number of symptoms including anemia, or are you really just trying to treat the anemia? And if one is just trying to treat the anemia, then a number of the agents we've talked about that can be used as single agents could be utilized. So erythropoietin-stimulating agents, immunomodulatory agents, and danazol – those things would be reasonable and appropriate in a patient whose principle issue was anemia. The second issue that has to be thought about before picking any treatment is: what is the impact of the anemia? Are we treating a number or are we actually treating something clinically meaningful? Now in a patient who is receiving blood cell transfusions, those are the patients for whom a treatment that is directed towards the anemia absolutely makes sense. We know patients who receive transfusions have a worse prognosis overall, not to mention the cost in terms of time and even the financial cost to the patient of having to come in for blood tests and transfusions on a regular basis. It's an enormous impact on the patient's life. Those are patients who should be treated for their anemia.

Dr. Turck:
And if we zero in on one of those considerations, Dr. Mascarenhas, how do you factor a patient's preferences into your approach?

Dr. Mascarenhas:
So definitely patient preference is a consideration. If you have a patient who lives a far distance and is not able to or willing to come to the cancer center on a frequent basis, and maybe that means even every three weeks, then perhaps an ESA may not be the best option for that patient unless they can receive it locally. Women who may be turned off by the idea of hirsutism should be a consideration, although I have to say that's usually not a major toxicity associated with danazol, but that's a consideration. And then, patients who have underlying issues of neuropathy – maybe a diabetic patient with neuropathy – that may not be the best patient to consider thalidomide as an option.

So really understanding the patient, their profile, their comorbidities, and their limitations or expectations with therapy will also help make decisions about which of the treatments might be ideal for that patient.

Dr. Turck:
Now we're almost out of time for today, so Dr. Rampal, I'll give you the final word. Given everything we've talked about today, can you tell us why tailoring treatment strategies for patients with myelofibrosis-related anemia is so important?

Dr. Rampal:
Trying to tailor the treatment for anemia in myelofibrosis is quite important because again, this is not a monolithic disease, and patients can have anemia and other symptoms, or they can have anemia in isolation or sometimes anemia and thrombocytopenia.

And now we are getting to the point where we have several agents that can address, let's say, these two different groups: patients with just anemia or patients with anemia and other myelofibrosis-related symptoms. So I think making that distinction early on will make a big difference in choosing the right therapy for patients.

Dr. Turck:
Well given that there are several factors to consider, I want to thank my guests, Drs. Raajit Rampal and John Mascarenhas, for joining me to share insights on their approaches to managing myelofibrosis-related anemia. Dr. Rampal, Dr. Mascarenhas, it was great having you both on the program.

Dr. Mascarenhas:

Thanks for including me.

Dr. Rampal:
Thanks for the opportunity to discuss these important topics today.

Announcer:
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