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Anemia and Myelofibrosis: Optimizing Diagnosis, Treatment, and Management Strategies

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

Dr. Turck:
This is *Project Oncology* on ReachMD. I'm Dr. Charles Turk, and joining me to discuss strategies for optimizing outcomes in patients with anemia and myelofibrosis is Dr. Prithvi Bose. He's a professor in the Department of Leukemia at the University of Texas MD Anderson Cancer Center. Prithvi, thanks for being here today.

Dr. Bose:
Thanks for having me.

Dr. Turck:
Well, to start us off, Prithvi, how do you evaluate the cause of anemia in patients who are newly diagnosed with myelofibrosis?

Dr. Bose:
Well, anemia, it's a very classic feature of myelofibrosis, perhaps not a hallmark because you don't have to have anemia, but it's very common. About a third of patients will have anemia at diagnosis, and then everyone will develop it at some point, so it's inevitable during the course of the disease. So when a patient presents, as you said, newly diagnosed with myelofibrosis, usually the anemia is from the disease. However, that being said, one always should do one's due diligence, which is to exclude bleeding, exclude deficiencies of iron or vitamins, i.e., nutritional causes. And yes, those are important to do, but the vast majority of the time when you encounter anemia in a newly diagnosed MF patient, the anemia is from the MF, and that could be due to bone marrow failure, which to some degree is present in most of these patients or which is just impaired red blood cell production in the bone marrow or accelerated destruction. You have some of thisineffective erythropoiesis going on. They could have an enlarged spleen with hypersplenism, and that could cause anemia. So there are different causes but they mostly come back to the disease itself, rather than extraneous causes.

Dr. Turck:
Now if we turn to the guidelines, what did they say about diagnosing and monitoring anemia in this setting?

Dr. Bose:
The NCCN, or National Comprehensive Cancer Network, guidelines that we follow here in the US have always had a separate page or an algorithm flow chart on managing anemia in myelofibrosis, again because it is such an important and common symptom. Now there have been certain recent changes to those guidelines reflecting, for example, the recent approval of momelotinib. But I think the big picture is that you always need to see what is the patient's main unmet need. And if it is anemia, we used to have a few options, although they were never specifically approved for anemia, but we always had a few options, which we still do, which are things like danazol, and then erythroid-stimulating agents and sometimes IMiDs, or immunomodulatory agents. And even luspatercept. Now note that none of these agents that I just mentioned is actually specifically approved for anemia of myelofibrosis, but they work. They work, and we've known that for some time, and one can use those as single agents if the patient's predominant issue is anemia, and we can sometimes use them with a JAK inhibitor if it is a patient who also requires a JAK inhibitor for say, relief of enlarged spleen or symptoms.

Now with the arrival of momelotinib, that latter situation is somewhat simplified because this is one drug which can address all of the three major manifestations of the disease, which are enlarged spleen, symptoms, and anemia. So now one could actually approach

those three problems in the same patient with one drug, whereas in the past, you would use these off-label drugs and add them to your JAK inhibitor or in the 20 percent or so of patients that only have anemia, you would use them singly.

Dr. Turck:
And how do you use those guidelines or otherwise determine which patients may benefit the most from treatment?

Dr. Bose:
Yes, this is of course, a very important question. It's a very key question because this is a very heterogeneous disease, and it's actually very different from perhaps any other cancer that we treat. You don't treat it by stage, you don't even stage it. You go according to the main clinical presentation of the patient. Is anemia their problem? Is the spleen their problem? Are the symptoms their problem? Are high blasts their problem? There could be many such flavors in which the disease presents. But of course, as you realize, patients are not usually going to come with just one problem. The same patient will have anemia, an enlarged spleen, some symptoms, perhaps a high white count. So there's all these different facets that we often see in the same patient. So the way I interpret the guidelines, which intentionally have been left relatively loose and broad, are to tailor the therapy to the patient, like I was alluding to earlier. If you're only treating anemia, then I think it is reasonable to use the anemia specific agents that I mentioned we've had for a long time, things like danazol, ESAs, luspatercept more recently. But if you have a patient who needs help with their symptoms and/or an enlarged spleen and is also anemic, then I think momelotinib lends itself really nicely to that setting.

An alternative would be to use ruxolitinib but add something for anemia because that drug, actually, not only does not improve anemia it actually worsens anemia.

Dr. Turck:
For those just joining us, this is *Project Oncology* on ReachMD. I'm Dr. Charles Turk, and I'm speaking with Dr. Prithvi Bose about the personalized treatment of anemia and myelofibrosis.

So, Prithvi, once you determine that a patient may benefit from treatment, are there any other factors that you take into account when developing an individualized treatment plan for them?

Dr. Bose:
Oh, absolutely. So one has to remember the big picture, which is that myelofibrosis is the most severe of the classic Philadelphia-negative myeloproliferative neoplasms. It has a median survival in the range of seven years, although, that varies widely. So I think the first question, when you're evaluating a newly diagnosed patient with MF, is to see are they a stem cell transplant candidate? And because of this, there are to this end, there are a number of prognostic models. So I think that's the first part of making an individualized treatment plan, as you alluded to because you need to assess their risk of dying from the disease and see if they need to be referred to transplant.

But once that is out of the way in the sense that most of us will refer to our transplant colleagues at that point but we still have to manage the patient's problems. So while that is underway, so to speak, the referral, the whole process of getting them ready if they're a candidate, we need to manage their clinical issues. So again, going back to what I said, this is a unique disease where you really treat according to the patient's clinical problem, and like I was alluding to earlier, that could be spleen, symptoms, anemia, something else.

Dr. Turck:
Now putting everything into perspective for us, Prithvi, what kind of impact could an individualized treatment plan have on these patients as far as, say, quality of life or optimizing outcomes are concerned?

Dr. Bose:
I think MF is really a disease where the individualization of the treatment plan is of paramount importance. I mean, we're all trained in oncology, or most of us are here in the US in hematology and oncology, and in solid tumors, this is from what I recall from fellowship and my early career. You usually have algorithms for what you give in frontline, what you give neoadjuvantly, or adjuvantly, what you give in second-line, third-line in the metastatic setting. But MF is very different. Again, you make that initial decision about do they need transplant or not? Is this the right time for transplant or not? But then, you start to focus on their clinical problem. You look at the tools we have, we have four approved JAK inhibitors. Each is a little different from the other. As I was alluding to, momelotinib has this nice additional anemia benefit as an example. Pacritinib can be used in patients with very low platelet counts. So they are somewhat different, whereas ruxolitinib and fedratinib are better suited to patients with preserved blood counts rather than those with cytopenias. So there are really many nuances that come in, and also, you've got to look at, again, not to belabor the point, but it's really important to focus on their specific clinical problem, and that's going to change over time. This is a chronic disease. You're going to follow them for hopefully a long period, and there will be new things that will emerge as the disease evolves.

Dr. Turck:

And finally, Prithvi, are there any other key takeaways on optimizing patient outcomes or any other aspect of managing anemia in MF that you'd like to leave with our audience today?

Dr. Bose:
Yeah, I think something I didn't touch on about anemia is that when it gets to the point that where the patient needs transfusions that is a significant burden on the patient, as well as the healthcare system. So some physicians will transfuse for less than eight hemoglobin, others will use less than seven. But regardless, the issue is that the patient does not feel good, they spend a lot of time in the office or in the hospital in that chair receiving the blood. It is certainly a burden on the healthcare system as well. So treatments for anemia are really very important for that reason as well. That quality of life or that healthcare economics reason as well.

And also important to say is that anemia has long been recognized as a bad prognostic factor. It features in every prognostic model we have, and the worse the anemia, the worse the prognosis. So it is an inherent feature of the disease, which imparts an unfavorable outcome to the disease.

Dr. Turck:
Well, with those final insights in mind, I want to thank my guest, Dr. Prithvi Bose, for joining me to discuss individualized treatment strategies for anemia and myelofibrosis. Prithvi, it was great having you on the program.

Dr. Bose:
Thank you, Charles. Enjoyed it.

Announcer Close
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