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Managing Myelofibrosis with a Patient-Centered Approach

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
Welcome to *Project Oncology* on ReachMD. I'm Dr. Charles Turck, and joining me to discuss how we can take a patient-centered approach to managing myelofibrosis-associated anemia are Drs. Justin Arnall and Jerry Spivak. Dr. Arnall is a Clinical Coordinator of Hematology at Atrium Health Specialty Pharmacy Service in Charlotte, North Carolina. Dr. Arnall, welcome to the program.

Dr. Arnall
Thank you for having me.

Dr. Turck
And Dr. Spivak serves as the Emeritus Professor of Medicine at Johns Hopkins University School of Medicine. Dr. Spivak, it's great to have you with us as well. So let's start with you, Dr. Arnall. How do you assess an AMIA severity in patients with myelofibrosis?

Dr. Arnall
Well, certainly when we're talking about anemia, we're we'll at hemoglobin hematocrit. And then right off assessing myelofibrosis as the cause of the patient's anemia, we're assessing the therapy that they're on. And then in terms of severity, we are looking at how symptomatic patients are and what symptoms they're expressing and how likely they are related to their degree of anemia. And with myelofibrosis, I think what's critical here or what's particularly useful here is performing an appropriate guideline-directed risk assessment, I think can give us a lot of useful practical insight into the patient's degree and severity of anemia and how effective we are in managing them.

Dr. Turck:
Now turning to you, Dr. Spivak, once you've determined the severity, how do you work with your patients to select the appropriate intervention?

Dr. Spivak
Well, I think the first thing you do is make sure the patient understands the disease. And the obligation of the physician is to be sure that he or she understands that has the correct diagnosis. And unfortunately, myelofibrosis has been dumbed down to one disease, so to speak, when there are three different NPNs, and they are genetically different. And this has been proven, but there are people who still hold to, well, essential thrombocytosis and polycythemia vera are different parts of the same disease when they happen to be genetically different diseases. And primary myelofibrosis is totally unrelated to those diseases. So you want to make sure the patient understands what they have, and you need to use the scoring system. If you want to stage patients, you need to use the scoring system that's appropriate to the disease. And as I've said before, people are not doing that, and that is a huge mistake.

And so because we've known about these diseases for most of them, for over a hundred years, so there is a track record, and you can spell it out for a patient, what exactly they're looking at. And if it's polycythemia vera or essential thrombocytosis, that's the marathon, not the sprint. And if it's primary myelofibrosis, there you have to be very prepared to separate out the patients who most need to be treated. And in the staging systems there's low risk, there's an intermediate one risk, there's an intermediate two risk, and then there's high risk. And as you get to intermediate two and high risk, these patients also have to be considered for bone marrow transplantation. And so then the question is in that you've got to be doing a number of things at the same time and patients have to be very well

educated as to what is going on and what they can expect.

The big question is how early do you start treating patients who have a diagnosis of primary myelofibrosis as opposed to those who have polycythemia vera with myelofibrosis. ET with myelofibrosis is rare if it is a JAK two mutation, and if in women, it's usually the men who get myelofibrosis. And then there are the patients with CALR or MPL mutations. But they're very small part of the number of patients. It's mainly the patients who have the JAK two mutations that can comprise the most patients that we're treating. But they all get treated the same way. So I think patient education is the first thing, and then understand who the enemy is. It's not the myelofibrosis, it's the stem cell.

Dr. Turck:
And after you've selected the right intervention, Dr. Arnall, what approaches do you take to monitor their response?

Dr. Arnall:
So again, one recommendation leads to another. And so using symptoms assessments in particular is helpful here. Obviously, also watching a patient's hemoglobin over time, watching their need for transfusions over time generally assessed on, I would say at least a quarterly basis potentially, more frequent depending on the intervention or depending on the degree of severity. And engaging a multi-disciplinary approach to watching symptoms, watching anemia over time is going to be important, and especially around the start of various interventions here.

Dr. Turck:
For those just joining us, this is *Project Oncology* on ReachMD. I'm Dr. Charles Turck, and I'm speaking with Drs. Justin Arnall and Jerry Spivak about patient-centered approaches to managing myelofibrosis-associated anemia. Now I'd like to switch gears and turn to some real-life patient cases from each of you. Starting with you, Dr. Spivak, can you tell us about a case that highlights how aligning with your patient's preferences impacted their outcome?

Dr. Spivak
Well, what I always liked to teach students and residents and fellows is that each patient with a myeloproliferative neoplasm is unique and how they respond to it. For example, women rarely get myelofibrosis very uncommon. More younger women get polycythemia vera than men do, and more women get ET than men do, and they respond differently. And so in terms of how you deal with your patients, each patient is unique. And for example, I had a patient come to me at age 29 with bone marrow fibrosis and a high platelet count and some splenomegaly. He did not, we thought at that time, have polycythemia vera. But then he had a splenic vein thrombosis, which made us realize he did have polycythemia vera, and I followed him until he was 62 with polycythemia vera from age 29 to age 62 with fibrosis.

And unfortunately, he would still be with us, but he developed hepatitis C from some blood transfusions following surgery. And the point I want to make there is that patients with myelofibrosis are not supposed to live that long. My favorite patient was a woman who had polycythemia vera, and she developed splenomegaly and thrombocytopenia. And she went to another medical center and was treated with an experimental tyrosine kinase before the tyrosine kinases were available on the market. And her thrombocytopenia became worse. So they stopped the experimental tyrosine kinase, gave her a drug holiday, and tried it again. And she still got severe thrombocytopenia. So she came to see us, and she had a platelet count that was, I guess in the 20, 30,000 range. And she was having trouble with splenomegaly. So I thought, all right, ruxolitinib had become available. I said, 'We're going to start you on ruxolitinib.' And we started on ruxolitiniband. Unfortunately, her platelet count went down to 10,000. So she had an excellent hematologist where she lived, and he agreed to give her platelet transfusion. She only needed two platelet transfusions. And over the course of six months using 10 milligrams of ruxolitinib twice a day, her platelet count came up over a hundred thousand, and her spleen started to shrink, and we kept her on the ruxolitinib, and she went into a complete hematologic remission. So that was 14 years ago when she'd already had polycythemia vera for 28 years. So you can do the math. When I last got her blood counts, and that was this year, she was still in complete hematologic remission. And so that patient defied theoretically what the norm would be. So you can never count patients out with this disease, and you try to treat each one of them, take what the disease gives you, and when you get into a complete remission status, don't change anything. And you can say, 'Well, that's E pluribus unum, one out of many.' But every patient has the possibility of doing what that patient does. Not everyone will, but I have many patients who have had their disease for over 40 years, and some of them have myelofibrosis. In fact, I would say probably all the polycythemia vera patients do. The primary myelofibrosis patients are not going to do that well. But again, they will surprise you upon occasion. So the idea is to be optimistic, take what the disease gives you, and run with that.

Dr. Turck:
And coming back to you, Dr. Arnall, is there an experience from your practice you could share with us?

Dr. Arnall:
Yeah, so in terms of monitoring follow up and engaging with patients, something that we've been able to do successfully here has been initiate a closer partnership between our clinic space and then our specialty pharmacy space where our pharmacists are actually engaged to help perform some of the symptoms assessments. The goal of this has been generally to offload some of the time in the clinics by having this performed prior to and outside, that way the clinic team and I can then focus on discussion intervention with the patients themselves. I think over time this can potentially develop into something more interventional depending on what patients and clinics need, and then the bandwidth of our specialty pharmacy.

But what I think we have seen through this practice of our specialty pharmacists performing MPN 10 symptoms assessments has been one, better adherence to this guideline recommendation, as well as I think a general utilization of the symptom scores. And then also overall a better degree of engagement by our pharmacy team within an awareness of these symptoms, how they have changed over time for individual patients and what not. So yeah, that I think that's been a particularly beneficial practice for clinic pharmacists and then ultimately patient.

Dr. Turck:
Before we end today, Dr. Spivak, how can taking a personalized approach to care have an overall impact on a patient's journey and outcomes?

Dr. Spivak
We have unfortunately, a test that can tell us, and it's not published yet, so I don't want to get anyone very excited, where we can tell who has polycythemia vera, this is, we can tell who is going to get, I don't want to say severe disease, but more complications from individuals who are not. And so I always look at polycythemia vera disease and go two ways. It can be extremely benign for decades, at least four decades, though I have one man, he has an unusual JAK two or uncommon JAK two mutation who started phlebotomies at age 17. I didn't see him till he was 71, so you can do the math there. He was still getting phlebotomies. He had some splenomegaly, but he was otherwise asymptomatic. So never misjudge what patients can do but take what disease is giving you.

And I think that's the most important thing in terms of precision medicine. We now have next generation sequencing. Unfortunately, this has not seeped down to the clinical level. When I suggest to patients who come to see me that they have their hematologist get next generation sequencing, many of them never heard of it. Although it is a clinically approved test, they don't, sometimes don't want to do it, don't understand what it means. But with next generation sequencing, you can get what we call a quantitative allele burden. And what that means is it can tell you how many stem cells actually have the disease. So in ET, say you'll usually see they may have an allele burden of 10 percent, which means 90 percent of their stem cells are normal. ET patients never have an allele burden greater than 50 percent. So as long as you're a chimera, you're going to have a normal lifespan.

PV patients unfortunately start out with less than 50 percent, but they go over 50 percent. So you won't know what the allele burden is. It's not so much important with the CALR mutation or the MPL mutation, but with the JAK two mutation, as long as you have less than 50 percent of your cells involved, that determines how you're going to treat the patients. And generally, unless they have itching or ocular migraine or something, you don't have to treat them with anything, except say if they have p vera with phlebotomy. And the phlebotomy, again, is precision medicine because in men, we know that as long as hematocrit is less than 45 percent, they're most likely 95 percent likely not to have a blood clot. Women are not small men, and no one seems to realize that they don't make the same androgen. And so we phlebotomies at Hopkins less than 42 percent, and we've known that since 1978, but you have a hard time convincing practitioners now because no one writes about how women are different than men. And to me, this is one of the great sins in the NPN field is treating everyone the same when every patient has their own story, their own genetics, and that will dictate their behavior more than anything else.

Dr. Turck:
Well, with those strategies in mind, I want to thank my guests, Drs. Justin Arnold and Jerry Spivak, for joining me to discuss patient-centered approaches to managing anemia and myelofibrosis, Dr. Arnall, Dr. Spivak, it was great having you both on the program.

Dr. Arnall:
Thank you so much.

Announcer Close
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