Transcript Details

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Challenges in Myelodysplastic Syndromes (MDS): Risk Stratification and Integrating Novel Treatment Approaches

Announcer Intro:
Welcome to CME on ReachMD. This activity, titled *"Challenges in Myelodysplastic Syndromes (MDS): Risk Stratification and Integrating Novel Treatment Approaches"* is Provided by Partners for Advancing Clinical Education (PACE) in partnership with Smart Patients and is supported by an educational grant from Gilead Sciences, Inc. and Karyopharm Therapeutics Inc.

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Dr. Sims:
Here are our disclosures, and these are the objectives for this session: to identify novel and emerging agents for LR and HR MDS treatment; to plan management strategies for AEs associated with novel therapies for MDS; and to integrate patient education and feedback to optimize the patient experience during treatment and survivorship. All right, I'm going to turn it over now to our speakers. Sara – Dr. Vance, welcome, and I'll turn it over to you.

Dr. Tinsley-Vance:
Thank you. MDS is one of my passions, so let's get started. First we're going to go over the prevalence and the risk factors and pathophysiology and symptoms. This is showing you that incidence and prevalence. So on the left, you have incidence. You can see it's slightly more for males than females, and prevalence as well. And overall, MDS is not like prostate and breast cancer, as you can appreciate on this slide. There's not as many of those patients. It is a disease of aging. On the left, you'll see those factors that go into the development of myelodysplastic syndrome. Aging – that predisposing mutation – sometimes patients are born with these mutations. We call those germ line. Environmental exposures – we're pretty familiar with that one. And radiation and chemotherapy. And then you get that hematopoietic stem cell or clonal expansion, you have the MDS initiating cells, and then patients acquire mutations over time. Those are called somatic mutations. Inflammation, microenvironmental changes, and then the patient develops cytopenias and can develop AML. MDS is a clonal – a spectrum, really. They're not all the same. They like to use the word heterogenous, so one MDS patient's case is not like the others, although you can group them, and that's what we're going to go over later. But it's a clonal, hematologic stem cell malignancy. It's not a disorder, it is really a malignancy. Many patients don't have symptoms at diagnosis, but as the disease progresses, their bone marrow stops working well and then you see cytopenias. This is what you see at the top – the clinical manifestations. Many patients are diagnosed when they don't have symptoms, because they have cytopenias, and that's detected during a routine lab draw. Many patients are going for their annual exams, or every 3 to 6 month follow-up, depending on their comorbidities, and that prompts a diagnostic workup. But in the second bullet, you'll see that many other patients do have symptoms, and they have the cytopenias, but they come to their doctor because they have symptoms, with anemia – which is the majority of our MDS patients, 90% of them. They have fatigue and exertional dyspnea, neutropenia – about 50% of them, with recurrent infections. And about 40% of them have thrombocytopenia and we all know that if your platelets don't work right and you have few of them, you're going to have problems with bleeding and bruising.

This is showing you how overall the U.S. population is aging. Aging and AML and quality of life – those are my areas of research. By

2030, 60 and older is going to be the biggest age group in the United States, and this is really speaking to that. We have better health and we have patients getting older. I have several 80+ year olds in my clinic. One on my study is 90 years old. It is, like we said previously, it's associated with aging, and you really need a comprehensive approach when you're dealing with an older adult. They have different goals, their comorbidities. We'll go over how you classify them and put them into groups, to better understand how to treat them. We talked about cytopenias on the left. Then you have to have a bone marrow biopsy with an aspiration, if possible, to diagnose them. Dysplasia, in 10% or more of the cells – that's a pathologist looking at the slides and seeing if they're dysplastic. Myeloblasts – they can have more than 5% but less than 20%, and I'm going to show you how that area is getting more and more gray as we go through this step. They have certain types of cytogenetic abnormalities, and there's evidence of clonality. But you have to rule out other causes, such as nutritional deficiencies – copper deficiency can look like myelodysplastic syndrome under the microscope – infections, substance abuse, and you can see those other ones.

We have a new classification system in 2022, and all of our pathologists are rushing to keep up with them, because they keep changing the criteria. This is the World Health Organization's 2022 classification of MDS, and what you'll notice in this is the incorporation in that fourth row. Mutations – SS3B1 and TP53 – reclassified a little bit based on those. And this is again showing you it's morphologically defined, but it has incorporated those mutations that we get from our mutation profiles.

And this is the International Consensus Classification, which is the new kid on the block, which really is making the lines between MDS and AML much more blurry, like we keep lowering the threshold for when we're going to treat patients aggressively. That's because our higher-risk MDS patients really behave more like an AML patient, as far as their prognosis. If you'll look at this, I'll just draw your attention to that blue banner across the top, 10% or greater myeloid blasts or blast equivalents in the bone marrow or blood, and you can see in the second box there, mutated TP53 with a VAF – or variable allele frequency – of 10% or greater – that's kind of a blurry line between MDS and AML. There's lots of discussion about this. There's a paper I'm involved in writing. Lots of back and forth about, are we really going to call patients who we previously called MDS, AML? And then what do you do with it?

So just for your information, we started with the International Prognostic Scoring system in 1997. We've moved on from there, and this categorizes patients as low, intermediate, or high, to know their bone marrow blasts, cytogenetic and cytopenias.

When you have that information, then you go across there and you see, does that person get a 0, a 0.5, a 1? And then you add them together and you come up with their score to know whether they're low, intermediate or high risk MDS. We have been really using the revised IPSS, which came about in 2012. Both of these by Dr. Greenburg – he's the one that put these together for us, which is very helpful. This now has more variables included in the revised version of the IPSS. We still have cytogenetics. We have blasts, hemoglobin, platelets and ANC, but you'll note that there is very low, low, intermediate, high and very high. What's difficult for a lot of us is what do you do with those patients, intermediate area? Are those low risk or high risk? So that's where we have now evolved into looking at it from a mutation standpoint – the IPSS and risk categories. So now, on those myeloid mutation panels, we take those variables and plug them into the risk categories, and we have a new strategy for being able to determine who really has higher risk disease. There's a calculator there at the bottom left, and I would encourage you all to get familiar with it, try plugging it in. Some of your patients that have high risk or intermediate risk on that IPSS-R, and see what you get for them. This has very low, low, moderate low, moderate high, high and very high. This is really just making that point and prove your familiarity with the updated risk assessment criteria because we're really going to this. Mutations make a difference.

This is what you need to calculate the IPSS-M. Blast percentage again, hemoglobin, platelets, cytogenetics, but you do need those gene mutations. And this IPSS-M does allow for missing data, so you can still get a score to be able to use that risk calculator.

These are the recurrently mutated genes that we know are involved in the pathogenesis of MDS. What I take away from this slide is wow, we've come a long way. And we've divided these mutations into their function. We have splicing factors, we have epigenetic regulators – TP53, which is universally bad – and then mutations in other genes only. And remember that these mutations accumulate over time, from a year to many decades, and sometimes when we treat patients, another mutation that we couldn't really appreciate before arises. So it's important to check those mutations again, if you're doing a repeat bone marrow biopsy, or even in the peripheral blood, to see if you have a change in your mutations that would change your management of your patient.

Now we have two big buckets that I'll talk about. We have lower risk MDS and we have higher risk MDS. That's how we divide our clinical trials into – whether our patient has lower risk or higher risk. What are your goals when you treat the patient? So with your lower risk MDS patients, on the left, you want to maximize their quality of life, you want to decrease their transfusion burden, improve their hemoglobin, and you want to make those cytopenias as minimal as possible.

And then, you want to attempt to reduce the risk of progression and improve overall survival, although some of our lower risk MDS patients live for many years. Whereas in higher risk MDS, you want to improve or maintain quality of life, delay progression, hit AML, and you also want to help them live a better life. We do still try to decrease transfusion burden in the higher risk group, but the key

takeaway is you really want to know whether your patient has lower risk or higher risk disease, and then discuss what those treatment goals are, from your perspective, with the patient. But maybe before that, talk to your patient, get to know them, ask them what their goals are. What's their most troubling symptom? How can you help them with that? Because you'll find that the patient and the physician frequently have different goals, and we really want to meet the patient's needs.

We'll start with a case study, Joe. He's 86 years old. I have some of these in my clinic. He has hypothyroidism, hypertension, renal insufficiency. His labs look like a typical MDS patient, with a hemoglobin of 8.7. You see that MCD is high at 107, so you know those red blood cells are big. Platelets are 159. Neutrophil count is 1.6. You do a bone marrow biopsy with aspiration – it's 70% cellular, so that's hypercellular for his age, and there's dysplastic terms in there that you can see, and he has some ring sideroblasts – 20%. No increased blasts, and his EPO level is 150. So the starting point with our MDS patient is erythropoiesis stimulating agent.

He has fatigue and worsening anemia 2 years later, and his hemoglobin has declined. He's now 7 grams per deciliter. White blood cell count and platelets are fine. His academic marrow showed MDS ring sideroblasts with multilineage dysplasia, so that means 2 or more lines – white blood cells, red blood cells or platelets – so 2 of those lines or more have dysplastic cells in them, and ring sideroblasts in 55% of his cells. Normal cytogenetic, and he has an SF3B1 mutation and a DNMT3A.

Lower risk MDS treatment paradigm consideration, so when you see a patient, you need to see, do they have symptoms? Do they have cytopenias? And then look at those mutations, see if they have higher risk mutations. And then, on that second row, you can see the cytopenias outlined. Anemia, thrombocytopenia, or pancytopenia with multilineage dysplasia. Depending on their cytopenia, that really drives what you do for the patient. With anemia, as we saw with Joe, you start with ESAs, and you give them transfusions to help improve their quality of life. If they have ring sideroblasts, like Joe had, you would start luspatercept, and if they had deletion of 5Q with anemia, you would begin with lenalidomide. If they have thrombocytopenia, you would start with a thrombopoietin agonist or a clinical trial. And for your pancytopenic patients, transfusions, ATT or clinical trial. I can tell you at our institution we really reserve ATG for use in patients who have a hypoplastic or hypocellular MDS.

And then you can work your way down the list, but you can see at the bottom, we still do transplant some of our lower risk myelodysplastic syndrome patients. This is a closer look at symptomatic anemia. We talked about ESAs, and then when you have transfusion-dependence, also know as failure of the ESA, we talked about for deletion 5Q you would use lenalidomide, nondeletion 5Q we also will use len, and then ring sideroblasts, SF3B1, luspatercept. And if they have adverse features of their disease, you may start with a hypomethylating agent.

This is showing you the response rate for ESAs. On the left, you see the growth factors. I'll give you a little bit of time to look at those. Sometimes you can add GCSF to erythropoietin and you get 47.8% response rate, but overall our response rates are between 15-40%. Again, just driving home this point, in order to really deliver patient-centered care, you have to know the patient and be respectful of and responsive to their preferences, their needs, their goals and their values so that you're focusing on what they hope to get out of their treatment.

Again, this is just further breakdown of your ESAs. I want to draw attention to duration of response in this slide, because your patients will want to know – how long is this likely to help me? With ESAs, it's around 1 year to 15 months. With luspatercept 30.6 weeks, so that's a pretty durable response, and foran – transfusion independence in 38% of it – patients. And for deletion 5Q, you can see that median duration of response is pretty good there – 2.2 years, but for non-deletion 5Q it was more modest with some responses. With our lower risk MDS patients, you want to set expectations and discuss this. It's an ongoing dialogue with your patient – how you're going to monitor them. You really want to decrease their transfusion needs, and their transfusion burden. You want to improve their quality of life so they can do the things that they enjoy. And overall, they have a lower risk of transformation to AML and you want to maximize that benefit.

We're going to talk about, again, luspatercept in greater detail. This is the treatment for a specific subtype of myelodysplastic syndrome. Those patients who have ring sideroblasts and have that SF3B1 mutation, who are transfusion-dependent, there's an escalating dose that's recommended in the package insert and was used in the clinical trials. It goes from 1 milligram per kilogram to 1.33 milligrams per kilogram, to a maximum dose of 1.75 milligrams per kilogram. It's a subcutaneous injection given every 3 weeks, and there are specific guidelines on how you increase the dose to maximize your benefit. Transfusion independence in 38%. Median peak hemoglobin increase is pretty impressive, at 2.55 grams per deciliter, so that's like getting more than 2 units of blood as a – a transfusion. And it has a favorable safety profile. It's subcutaneously rather easy to administer.

And this is showing you, from the MEDALIST trial, which is what led to the FDA approval, comparing luspatercept to placebo in MDS patients who were transfusion-dependent, and this is showing you how they became transfusion independent. Luspatercept is in blue and placebo is in purple, and you can see who the winner is here, thus it was FDA-approved.

These are the side effects that you want to become aware of, make yourself familiar with them so that you can educate your patient when they say, okay this is what our goal is but what can I expect when you start this. Fatigue is a tough one, and I see this in clinical practice. So really, that gets that – setting that expectation at the top. 27% of the patients had any grade. But you can see over on the right that 3% of them had grade 3, so that's pretty significant fatigue. Then you can work your way down the list – diarrhea, asthenia and nausea, dizziness. From my perspective, I think that the fatigue has been my most difficult one to overcome with patients in discussing it, because they're already severely fatigued.

So there's another study coming in for up-front luspatercept, compared to epoetin. You can see on the left the criteria for being enrolled in this trial, and how patients are randomized to luspatercept compared to erythropoietin. And they're looking for 12 weeks transfusion independence, with a mean hemoglobin increase of 1.5 grams per deciliter. So we'll look forward to this ongoing study to see if we can use this up front.

This is taken from ASH abstracts that were presented on real-world data, retrospective on the left, and again, a retrospective review on the right. The one on the left had 114, RBC transfusion burden 47%, dose escalation 55 – so the majority needed an increase in their dose. And higher response rate were associated with lower transfusion burden at baseline, and this is consistent with what we know from the MEDALIST trial, and the takeaway from that is don't wait until your patient is heavily transfusion-dependent to start them on the appropriate therapy, because you get a better response if you start them before they've had multiple transfusions. 39.5% hematologic improvement, and the median duration of response is 15.6 months. And on the right, you can see how those results play out. Median duration of transfusion independence was 27.9 weeks, so really this is our new kid on the block. You want to make sure you're aware of it, and use it for patients that meet the criteria that it's intended to be used for.

So now let's look at lenalidomide versus placebo. This is an older study. It was a randomized, double blind, phase 3 trial in transfusion-dependent patients with deletion 5Q, mutated MDS. The most common grade 3 AEs were neutropenia, thrombocytopenia, leukopenia, anemia and DVTs.

And you can see that on the right there, that the response correlates with the dose of lenalidomide, with the green bars representing 10 milligrams of lenalidomide. So just to be aware that responses are related to the dose that you're able to administer.

So now let's turn to higher risk MDS. We're going to start with a case study. This is Pearl. She's smiling even though she has higher risk MDS, which is amazing to me – our patients who have really bad disease that encourage us. She is 76. You can see she has a lot of symptoms. Had waldenstrom's macroglobulinemia. Treated with chlorambu and prednisone for 2 years, but then comes in and has a white count of 22,000, blasts of 2,170. So you can see that she's got higher risk disease, just from this. Platelets were 13,000. Her bone marrow showed – this is an old classification system diagnosis – refractory anemia with excess blasts too. 18% myeloblasts. So she was evolving into erythroleukemia and she has a complex karyotype. How do I know that? If you look at the cytogenetics, there are 3 or more cytogenetic abnormalities, and when that occurs, we know there's a high incidence of TP53 mutation and that's what she had. So I'll turn it back over to Taren.

Hypomethylating agents are the standard of care for higher risk MDS patients, and this is showing you on the left the median overall survival, when you compare azacitidine treatment to conventional care regimens. Overall survival was 24.5 months compared to 15 months. We know that some of the problems with the decitabine on the right is the way the study was run. In many instances, at our institution we use azacitidine over decitabine, but we use both agents. Looking at the phase 3 AZA-001 study, which had 358 patients, again showed 2-year overall survival superior with azacitidine 55%, and no significant differences in the rate of bleeding or infection. So again, azacitidine in hypomethylating agents are our backbone, and then the clinical trials usually add something to that, and we'll see that as we go through these.

This is how it's dosed. I'm sure many of you are aware of this. 75 milligrams per meter squared, subcutaneously or intravenously. We really want to stress that for higher risk disease, you want to use those 7 consecutive days, or 5 consecutive, 2 off for the weekend and 2 the next day has been shown to be equivalent. You want to premedicate your patients for nausea and vomiting. You repeat the cycle every 28 days, and you want to wait until your patients have 4-6 treatments before you determine if they've had a response. And you have to monitor them for constipation. Some of that goes along with our antiemetics too, but definitely it's a side effect of azacitidine. Usually during the first 2 cycles, things will get worse before it gets better, and that's where you really have to educate your patient. Watch for renal toxicity, and you want to check your patient frequently, so that you keep them safe.

These are the adverse events. Nausea – we do a pretty good job with antiemetics, so that's not really much of a problem at our institution because we use antiemetics. Anemia, thrombocytopenia, some vomiting, just so you're aware of these. Overall survival in high risk MDS remains very poor, despite HMAs, and you can see that that's a problem that we're trying to address by that ICC, where we're lowering the threshold where we try to treat them more like AML patients. So you can see the survival curves, they're right on top of each other with azacitidine versus decitabine on the left. And then, median overall survival is usually measured in months, not years,

and that could be a difficult discussion with your patient.

Back to Pearl – she wants to be considered for a clinical trial. She thinks that's her best bet. She's read up on clinical trials, and you log on to clinicaltrials.gov to facilitate referral. Some of you may think this is crazy, but I've done this for patients, where we don't have the clinical trial here that would be best for their disease. And for Pearl – she was enrolled in a clinical trial using magrolimab and azacitidine. So, the backbone azacitidine plus something else. And we know that the early phase trials of mag plus aza have shown activity to NTP53 mutated MDS.

This is showing you the rationale for CD47 blockade in high risk MDS. On the right, those leukemic stem cells – there are more of those CD47-positive cells. And then, on the left there, you can see it's the Do Not Eat Me signal on the cancer cells. So if you use magrolimab, and you block that Do Not Eat Me signal, then the second part of that picture, or cartoon, shows that macrophage engulfing that cancer cell, and that's how it works. The one drawback to magrolimab is you also have CD47 on your old blood cells, so you can get a big drop in the hemoglobin when you initially start a patient on therapy.

And this is showing it from phase 1B studies. Dr. Soliman works here at Moffitt with us, using magrolimab plus azacitidine in our higher risk patients. On the top you see overall response rates, with TP53-mutant MDS patients on the far right column. And you see 68% overall response rate, 40% CR rate, and you can go on down the line, and median overall survival of 16.3 months. But, what you want to also pay attention to is that for all comers, the median overall survival has not been reached. That means those patients are still alive, so that's very encouraging. Even for our TP53-mutant patients, it's better than what we've had.

You can see from this slide that AEs – constipation, thrombocytopenia, anemia, neutropenia. Median hemoglobin decrease from baseline to first dose was 0.7 but the range was a decline of 3 grams, to 2.4 grams per deciliter. So, monitor your patient closely, especially in the beginning and transfuse them.

One strategy we used at our institution is we transfused them at a higher threshold, anticipating a decrease when we treat them.

And then the ascertain is looking at a different agent. The efficacy of oral decitabine-cedazuridine. Cedazuridine in patients with MDS and CMML, and then you can see these results here. Median duration 14 months. This is an oral agent, so it gives you more flexibility in treating your patient. An oral hypomethylating agent, but you still have to monitor them for declines in the blood counts. And this is showing you how those AEs pan out – neutropenia, thrombocytopenia and anemia – and then if you look at grade 3 or greater, on the right column there, it's right around 50% for neutropenia and thrombocytopenia, and then anemia is behind it.

So this is the safety information. It's consistent with what we see with IV decitabine. They're thought as comparable based on the study, and most grade 3 or greater AEs are hematologic. So monitoring your patient, setting expectations, keeping them safe.

And then, for dose reduction for myelosuppression, with the oral decitabine- cedazuridine, the recommended dose – it is a tablet – days 1 through 5 of a 28-day cycle, and then it's 35 milligrams of decitabine with 100 milligrams of cedazuridine. And no food for two hours before or after the dose, again monitoring them. CBC prior to therapy and prior to each cycle, and you want to delay the treatment if the neutrophils are low – less than 1,000 – or platelets are less than 50,000. And then, there are dose recommendations – dose reduction guidelines, so just pay attention to those.

This is showing you investigational drugs that are used in combination with hypomethylating agents. You see sabatolimab, FLT3 inhibitors plus an HMA, magrolimab which we went over, and venetoclax. Some of these are fairly farther along in trials. Magrolimab and venetoclax-azacitidine, just to make you aware of them. Talk to your patients about clinical trial enrollment. Especially we want to encourage not just white people to be enrolled in clinical trials, and if you have a patient of a different ethnicity, talk to them more to see why they don't want to participate in trial if they tell you no.

And then we have oral azacitidine as maintenance therapy after transplant. This is a phase 1-2 study of oral azacitidine. You may know it as CC-486. It's dosed 200-300 milligrams daily for 7 days, or 150-200 for 14 days for a 28-day cycle.

There are going to be more clinical trials with this in a phase 3, comparing oral aza versus placebo for maintenance, and that is currently recruiting in the United Kingdom.

And these are other agents that are targeting that CD47. Remember that's the Do Not Eat Me signal. At the top, you'll see magrolimab and evorpacept. And RBC-sparing they are not. But as you go further down the list, you can see that these last 5 are red blood cell-sparing, so you wouldn't have to worry about that dramatic decrease in hemoglobin, and then you can see that they are at the beginning stages of being researched in phase 1 trials.

And then, eltanexor. Remember, this is our nuclear export inhibitor for HMA-refractory. It's an oral agent. It's less emetogenic than selinexor, if you're familiar with that, that's used in multiple myeloma. It's in phase 1-2 studies for intermediate 2 and higher MDS

patients who have 5-19% blasts, or higher risk MDS. And they have 50% response rates – you can see those for the 20 milligrams dose, and 60% response rates for the lower dose of 10 milligrams, but you will note that those are low numbers, so more to come, stay tuned.

This is showing you a phase 1B study of venetoclax in combination with aza for relapsed/refractory MDS. And this is really trying to determine what the best dose is, so you'll see 400 milligrams, 200 milligrams, 100 milligrams, to go to the safety expansion and they are also looking for overall response rates and hematologic improvement. This is for our higher risk MDS patients. Venetoclax in combination with aza for relapsed/refractory MDS, looking at the response and durability there. So pretty impressive – 39%. This is looking at phase 1B study of venetoclax in combination with aza for relapsed/refractory MDS patients. Transfusion independence and hematologic improvement on the left. They have it broken down by mutations. What you'll see is that IDH2-mutated patients are having the best responses – 83%. And then transfusion independence and hematologic improvement on the right – you can see those are pretty respectable numbers for MDS treatments. And then venenasia in high risk MDS – the M.D. Anderson experience – overall responses, looking at that. Pretty impressive.

And then we're going to talk about sabatolimab, which is a TIM-3 inhibitor. It's really helping your immune system take care of your leukemia cells. Kind of similar in concept to magrolimab but it works differently on this TIM-3 inhibitor. So T-RAGs, and effector, tilisalis-UC those are part of your immune system. And then you see your tumor cells.

This is the study design. It's multi-centered. Dose escalation, phase 1B. Decitabine with sabatolimab and azacitidine, and they're looking for maximum tolerated dose. Recommended dose, safety and tolerability, and then these are some of the response rates and durability, which are pretty impressive. If you look on the left, median duration of response is 21.5 months for your TP53, and then 16.1 for your adverse risk mutations. And then on the right, you see those results also, and then we have stimulus MDS1. This is first line therapy that was presented at ASH.

And now let's just talk for a couple of minutes about the disparities in MDS. We don't have enough data and again, that push for including your patients of different ethnicities in our clinical trials, and if they say no, trying to understand why they say no. This is a study that showed from SEER data that for black patients diagnosed with MDS, they had a longer survival and refractory anemia with ring sideroblasts and MDS not otherwise specified, also favored black patients, whereas refractory anemia with excess blast subtype favored survival of white patients. The more we learn, the more we have data, we can understand differences better, and really try to get at what the underlying cause is. One of my areas of research is sex disparities in outcomes, and I took a look with Dr. Komrokji in our leukemia group on our MDS database that has over 4,000 patients, and noticed that men have more splicing machinery mutations, and we think that's what really show that they have inferior survival, especially in our lower risk MDS patient. And women have more 5Q-deletions. There was more therapy-related MDS from our breast cancer patients who have been treated, and they generally have a superior response to ATG and cyclosporin, and they have more hypoplastic MDS – or hypocellular MDS.

Thank you so much for your participation, and this is our action plan. We want to really improve your familiarity with these updated risk assessment criteria, and be able to identify how the goals are different between lower risk and higher risk disease, know the common side effects of luspatercept, and mitigation strategies. And please, discuss clinical trial enrollment with your patients with higher risk MDS. Thank you.

Dr. Sims:
So here's the question, Sara. This is a provider who says we dialyze an 80-year-old patient with MDS who gets transfusions every 6-8 weeks. We give Venofer q. treatment due to low ferritin and T-sats. The hemoglobin goes up to 8 and then starts dropping below 7. This is always her trend. There is no improvement. What could they do in dialysis to help this patient, if anything?

Dr. Tinsley-Vance:
That's a really good question. You know, your kidneys make your erythropoietin that tells your bone marrow to make red blood cells, so if the patient is not on any type of erythropoietin, you want to make sure that you have enough iron, and then you want to give her what she's not making on her own because her kidneys are not working.

Dr. Sims:
That's a great question. And I have one to go with it briefly.

Dr. Tinsley-Vance:
Okay.

Dr. Sims:
How low could a patient's hemoglobin go before transfusion in your practice?

Dr. Tinsley-Vance:
The patients don't like that the threshold was decreased to 7 grams, but that was in patients who are in the hospital. I make individual decisions. I don't have like a set number, although for our institution, if they're 7 or less they can get a transfusion. But I have patients who have cardiac issues, who have pulmonary issues, that we've set a higher threshold for them and as long as I justify it in my note – we do have people who check to see that you're using blood with some discretion – I've never gotten into trouble for transfusing at a higher threshold. I like to use 8 or 8.5 on people who just cannot hardly walk when their hemoglobin gets below that.

Dr. Sims:
Welcome to the PCE 2023 Oncology Winter Conference. I'm Terran Sims, your moderator. I'm a nurse practitioner in the Department of Urologic Oncology at University of Virginia in Charlottesville. Our first topic is challenges in myelodysplastic syndromes, or MDS, risk stratification, and integrating novel treatment approaches. And our first faculty is Sara Tinsley-Vance. She's a Ph.D., APRN. She's a nurse practitioner and researcher in malignant hematology at the Moffitt Cancer Center in Tampa, Florida.

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