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The Bloodline with Blood Cancer United Podcast

A Podcast for Patients and Caregivers

Episode: 'The Bloodline Live! Myelodysplastic Syndromes (MDS) Updates in Research'

Description:

Curious about what's new in the world of myelodysplastic syndromes (MDS)? We're bringing you the latest insights straight from one of the field's leading experts.

In this episode, we speak with Dr. Mikkael Sekeres, of the Sylvester Comprehensive Cancer Center at University of Miami Health. Recorded onsite at the 2025 ASH (American Society of Hematology) Annual Meeting and Exposition, this conversation explores what MDS is, how it's treated today, and what researchers are learning about managing side effects.

Dr. Sekeres also walks us through the most notable MDS updates presented at ASH, highlighting promising therapies and clinical trial data that may help shape future care. Whether you're newly learning about MDS or following ongoing research, this episode offers an accessible look at where things stand and what's on the horizon.

*This is not an official program of the ASH annual meeting

Transcript:

Elissa: Welcome to *The Bloodline with Blood Cancer United*. I'm Elissa. Thank you so much for joining us on this episode.

Today we are speaking to Dr. Mikkael Sekeres, Professor of Medicine and the Chief of the Division of Hematology at the University of Miami Health System and Sylvester Comprehensive Cancer Center in Miami, Florida. Dr. Sekeres' research focuses on patients with myelodysplastic syndromes, or MDS, and older adults with acute myeloid leukemia, or AML; and he has been the national and international primary study investigator on dozens of clinical trials. You may recognize Dr. Sekeres from when he joined us on a June 2023 video series with MDS patient Caitlin discussing treating and living with MDS. Welcome, Dr. Sekeres.

Mikkael A. Sekeres, MD, MS: Thank you so much for having me back.

Elissa: So, we are actually onsite today at the ASH Annual Meeting and Exposition presented by the American Society of Hematology. This is a huge conference where oncologists and researchers from around the world are presenting on clinical trials and emerging therapies for all different types of blood cancer.

We are excited to talk to you today about the latest advances in treatment for myelodysplastic syndromes or MDS that have been shared at this conference. But before we get into that, let's start with the basics. Could you tell our listeners what MDS is?

Dr. Sekeres: Sure, well MDS, or myelodysplastic syndromes, is considered a type of cancer of the bone marrow. Now, there's a wide spectrum of severity of

myelodysplastic syndromes, so at its lowest forms, it may cause some mild anemia and not a lot of symptoms and may just be picked up on a routine blood test that leads to a bone marrow biopsy. The diagnosis can only be made with a bone marrow biopsy.

At its more severe forms, myelodysplastic syndromes can resemble acute myeloid leukemia; and, obviously, we treat it very, very differently, whether it's a lower-risk, less worrisome myelodysplastic syndrome versus something that's closer to acute leukemia. A myelodysplastic syndrome that's less worrisome, some patients we can even watch and wait and not do anything other than support them as they may not even require blood or platelet transfusions.

One of my patients once referred to that as having mild displeasure syndrome. He didn't like having to fight through the traffic to come see me in clinic; but other than that, the myelodysplastic syndrome didn't have much of an impact on his life. For more severe forms like acute myeloid leukemia, we have to start therapy almost immediately.

Elissa: Okay, so what are the current treatments for MDS?

Dr. Sekeres: Once again, it depends on what type of myelodysplastic syndromes you have. So, one of the first steps we take when someone is diagnosed with myelodysplastic syndromes is determining what their International Prognostic Scoring

System or IPSS score is. We have the most recent version of the IPSS, which is referred to as the IPSS-M or IPSS molecular. And that serves as almost a default staging system for my patients. So, a lot of my patients may not know somebody who has myelodysplastic syndromes, but they know someone who has, for example, breast cancer; and they know that that person's breast cancer has a stage. This is our way of staging myelodysplastic syndromes; and the higher the score, the more advanced is the myelodysplastic syndrome and the more we have to start a therapy.

Now, that can get pretty complicated. In fact, even I have to enter a lot of data online to a centralized website to generate an IPSS-M score. So, we simplify it even for ourselves and divide MDS into people who have lower-risk disease or higher-risk disease. Those patients who have lower-risk myelodysplastic syndromes, who have lower scores, we can treat with a variety of drugs. Sometimes we don't need anything at all, what we call active surveillance. Sometimes we have to give a blood or platelet transfusion every so often, but it doesn't affect someone's quality of life. And sometimes we have to address the predominating blood abnormality that's having an impact on their lives or requiring blood or platelet transfusions.

So, for example, somebody who has anemia associated with lower-risk myelodysplastic syndromes we might treat with an erythropoiesis-stimulating agent, which is just a hormone. And that can work in about 40% of people who are treated. Some people we might treat with the drug luspatercept, which works on more

advanced stages of red blood cell formation, and that's a shot that's given every three weeks or so; and that may have as much as a 60% chance of working.

For people for whom those drugs don't work, we then turn to other drugs to treat lower-risk myelodysplastic syndromes. Those might include drugs like imetelstat, which has been the most recent drug approved by the FDA for treating lower-risk myelodysplastic syndrome. For higher-risk MDS, we start to use low doses of chemotherapy, a class of drugs we call the hypomethylating agents. Those include azacitidine, decitabine, or a pill form of decitabine called decitabine-cedazuridine. It's higher-risk patients we also start to consider for a bone marrow transplantation. The only cure for myelodysplastic syndrome is a bone marrow transplantation, but we tend to offer it only to our patients with higher-risk disease because the side effects to the transplant can be quite significant.

Elissa: Could you tell us about the side effects of these treatments, and are they manageable?

Dr. Sekeres: They're absolutely manageable. So, side effects for drugs that are used to treat lower-risk myelodysplastic syndromes tend to be less because we adjust the drugs that we use for lower-risk myelodysplastic syndromes commensurate with the severity of the diagnosis. So, lower-risk diagnosis, we don't want as many side effects or we're not willing to tolerate as many side effects.

So, very few side effects with drugs like erythropoiesis-stimulating agents, the hormone I mentioned to treat anemia, or luspatercept, which is also used to treat anemia. Some of those side effects could include things like headache or dizziness. We also don't let the hemoglobin go too high when patients are treated with those drugs because of the risk of developing blood clots. It's more of a theoretical risk. We really don't see the development of blood clots very often in patients with myelodysplastic syndromes, but we also don't want to risk it. So, we keep the hemoglobin at a maximum of about 12.

Once you get to drugs like imetelstat, you start to see some side effects of the drug causing some worsening of blood counts, not the anemia – that's what it's meant to fix – but with lower platelet counts and lower white blood cell counts.

We also have the drug, lenalidomide. That's approved by the FDA to treat a very specific subset of lower-risk myelodysplastic syndrome, and that's MDS-associated with a deletion 5q genetic mutation. In those patients, lenalidomide can work quite well – in fact, in about two-thirds of patients. However, it also is associated with the side effect, like imetelstat, of lowering the platelet count and the white blood cell count.

Elissa: Okay.

Dr. Sekeres: For patients with higher-risk myelodysplastic syndromes, our go-to drugs tend to be the hypomethylating agents, like I mentioned before, azacitidine, decitabine, or the pill form of decitabine which is decitabine, joins to the drug cedazuridine. All of those drugs, the major, major side effect to them is that they can make the blood counts worse before they make them better.

So, I usually have a discussion with my patients about this fact and ask if they're willing to stick it out for a good four to six months of therapy. We need to give these drugs a little bit of time to work before we declare a victory or defeat. And about 90% of people who are destined to respond to a drug will do so within the first six months. So, I ask my patients to stick it out for six months. If a drug doesn't work by that point, it's unlikely to work.

Elissa: Okay. So, when you're talking about decreasing blood counts and affecting the blood counts, so then are they generally getting transfusions through that time?

Dr. Sekeres: They may. So, people who start out requiring transfusions are more likely, of course, to continue to need transfusions until the drugs actually work. I will tell you when I first meet a patient, it's very difficult to determine whether that person is going to have more profound drop in their blood counts or less profound or not even much of a drop in their blood counts at all. So, I prepare my patients that there may be the possibility that they'll need blood transfusions and platelet transfusions or that their

immune system may go quite low, in which case we may need to start some antibiotics to help prevent infections from occurring.

Elissa: So, then after that six-month period, if you found that that doesn't work, then what is the next step for patients?

Dr. Sekeres: Once again, it depends on what type of risk MDS they have. Patients who have lower-risk MDS, who might start with either an erythropoiesis-stimulating agent or a luspatercept, may then turn to a drug like imetelstat or they may turn to a drug like lenalidomide. We even do use the hypomethylating agents in patients who have lower-risk MDS, although from research that we helped conduct, we realize that we have to give lower doses of the hypomethylating agent than we do for patients who have higher-risk MDS.

Once a patient has higher-risk MDS and are treated with hypomethylating agents, we really don't have a lot of great options after that fact. We try to get these folks to a bone marrow transplant, like I said before, the only chance that we can cure their MDS; or we may have to turn to stronger chemotherapy to try to control their MDS.

Elissa: Okay, let's discuss the future of MDS treatment. Are there any emerging therapies or clinical trials that you're excited about, particularly those that have been presented on at this conference?

Dr. Sekeres: Sure, well there were a couple of neat presentations on new drug approaches that are being explored for MDS. One is of a drug called elritercept, and that's almost like a next-generation luspatercept. So, we're excited to see if that drug works even better than luspatercept and, in particular, works in patients who have a subtype of myelodysplastic syndrome that does not include ring sideroblasts. Luspatercept works particularly well in patients who have ring sideroblasts. We're looking for a drug that'll work just as well but in patients who don't have the ring sideroblasts.

There was another drug that was presented by a company called Rigel that was referred to as an IRAK 1/ 4 inhibitor that shows a lot of promise in patients who have been treated with other drugs previously. So, we're starting to see drugs that are being pursued for patients who've already been exposed to other drugs in the lower-risk setting. We continue to see the emergence of combinations of therapies, so drugs that are combined with azacitidine or decitabine for patients with higher-risk MDS. We were disappointed by recent data that came out that showed that the combination of azacitidine with venetoclax, which is the standard for patients who have acute myeloid leukemia actually doesn't work any better than azacitidine alone in patients with higher-risk myelodysplastic syndromes; but there are other drugs that are now being combined with azacitidine, and we keep crossing our fingers that one of

these will hit, and we'll have our first combination therapy standard for higher-risk MDS.

Elissa: Wow. That would be just so exciting.

Dr. Sekeres: Yeah, it would be amazing.

Elissa: Well, it sounds like it's been a great conference then with a lot of new things coming out.

Dr. Sekeres: It's incredible. There are 30,000 people here in Orlando. I just wish it were a little sunnier.

Elissa: Yes, a little sunnier would be very nice.

So, our final question for you today, on our patient podcast home page, we have a quote that says, "After diagnosis comes hope." What would you say to patients and their families to give them hope after a diagnosis of MDS?

Dr. Sekeres: Well, my word, not all MDS is the same. There's a wide range of severity of MDS, and we have a lot of treatments that we can offer to people. So, the very first step after getting a diagnosis of MDS is to get a lot of knowledge about the type of MDS you have and what those treatment options are. I highly recommend that people go to MDS specialty centers. We did some research through the National Institutes of Health (NIH) that showed that there can be differences in diagnosis for somebody

with MDS if they go to a local center versus a specialty center of as much as 20%. So, one out of five people will have a diagnosis that's changed; so, please, please, please get to an MDS specialty center. Go for a second opinion, and have that bone marrow interpreted by a pathologist who really has specialty in myelodysplastic syndromes.

Elissa: That's a very good point. Now, since you say that, for patients who may live in a more rural area or away from a research hospital, they may be hours away, is it possible to potentially have a local oncologist and then connect with a specialist at the same time at the research hospital?

Dr. Sekeres: Sure. And I would certainly look into telemedicine options, right? Particularly within the same state, you can have a telemedicine appointment with a doctor at an MDS specialty center. It's always worth your time to have that second opinion.

Elissa: That's good to know.

Well, thank you so much, Dr. Sekeres, for joining us today and telling us all about these exciting developments here at ASH and about the current treatments, of course, as well. It sounds like there is so much hope in the MDS world for the future and to get patients better.

Dr. Sekeres: Well, gee whiz, thanks so much for having me.

Elissa: Yes, thank you.

And thank you to everyone listening today. *The Bloodline with Blood Cancer United* is one part of our mission to improve the quality of lives of patients and their families.

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We would also like to know about you and how we can serve you better. The survey is completely anonymous, and no identifying information will be taken. However, if you would like to contact Blood Cancer United staff, please email, TheBloodline@bloodcancerunited.org. We hope this podcast helped you today. Stay tuned for more information on the resources that Blood Cancer United has for you or your loved ones who have been affected by cancer.

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