

Treating MDS

TRANSCRIPT

Caitlin
MDS Survivor

Are there different types of myelodysplastic syndromes (MDS) and are they treated differently?

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There are, and this is where things get a little complicated. And I honestly feel bad for my patients who are given this diagnosis and then do research online. And if I were in their shoes, I think I'd get awfully confused awfully quickly. One way that we classify myelodysplastic syndromes is what it looks like to a pathologist, a doctor who looks at the bone marrow, and that's classified by the World Health Organization (WHO), and they divide it into a number of different subtypes. Some patients may have MDS with uni-lineage dysplasia, meaning one cell line is abnormal. Maybe it's multi-lineage dysplasia, multiple cell lines are abnormal. Maybe it's a hypoplastic MDS, meaning that it's an unusual subtype of myelodysplastic syndromes where there aren't a lot of cells in the bone marrow. Or sometimes people have MDS with increased blasts. Blasts are immature white blood cells. It's normal to have fewer than 5% blasts in the bone marrow. People who have 5 to 9% blasts or 10 to 19% blasts have too many. And we would say they are classified as having increased blasts. So that's one way of classifying myelodysplastic syndromes – by the pathology.

One of the most common questions I get from my patients is they will ask me, “What stage am I?” We've just talked about how MDS is a blood or bone marrow cancer. People know other friends who have cancer, or they may have had cancer themselves and they say, “Well, I have a friend who has breast cancer and she's stage II.” Or “I have a friend who has lung cancer and he's stage III. What stage am I?” We don't have a formal staging system for myelodysplastic syndromes. And the reason is that it's in our entire bone marrow. It's in our entire bloodstream. So, everyone would be stage IV.

So instead, we use something called the International Prognostic Scoring System. And what that does is looks at three areas of a person's diagnosis. The first is the percentage of blasts that a person has in the bone marrow. The second is the degree of anemia, low platelets, or low white blood cell count that a person has. And the third are the genetics of that myelodysplastic syndromes. We plug this information into an online calculator, and it spits out a score and that score helps us to “stage” myelodysplastic syndromes. In broad strokes, we divide it into lower-risk myelodysplastic syndromes or higher-risk myelodysplastic syndromes. And that helps us determine what therapy someone should receive, and also, that person's prognosis.

Caitlin

So, what are some of the side effects for various treatment plans?

Dr. Sekeres

You know, it's an interesting question. When we think about starting a therapy in somebody who has lower-risk myelodysplastic syndromes, we do a little bit of an analysis comparing the quality of life that somebody has right now versus what that quality of life might look like on a medicine. So, for somebody like you who has a good quality of life right now, you feel good, you're actively raising two young kids and don't have side effects to your myelodysplastic syndromes, your quality of life would be like up here. So, if I add a medicine, I'm not going to raise that quality of life any more, but I might

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give you side effects to that medicine. So, that's why we don't start a medicine until somebody absolutely needs it. On the other hand, somebody who, for example, is requiring transfusions every week or two, doesn't have that great quality of life. If their quality of life is down here and I start a medicine, I might be able to raise that quality of life higher, and the side effects of that medicine hopefully won't offset that.

So, some of the side effects that we see can be very minor. Sometimes we treat anemia with hormonal therapy. We give recombinant humanized erythropoietin (rHuEPO), that's the generic name for it, or we give darbepoetin, a long-acting version of that and they often don't have a lot of side effects to them. On the other hand, there are some drugs that we give where we actually make the blood counts worse before we make them better. So, somebody might for a period of time actually require more blood transfusions or more platelet transfusions or their immune system may drop, and we have to put them on antibiotics to help prevent infections. So, we always weigh the side effects of these drugs against a person's quality of life to make sure that we're not negatively affecting that.

I've now had the privilege of treating people who have myelodysplastic syndromes for 20 years. And believe it or not, when I started, there were no therapies approved by the FDA (United States Food and Drug Administration) for the treatment of myelodysplastic syndromes. The very first one was in 2004 that was azacytidine, and it was followed a couple of years later by decitabine and the drug lenalidomide.

Then, there's been a huge gap in time before there have been other drugs approved for the treatment of myelodysplastic syndromes, including luspatercept and an oral version of decitabine, so people can now take pills instead of needing to get an intravenous injection. And we have more coming on the way.

So, the landscape of treating myelodysplastic syndrome is very, very different than when I started 20 years ago. What's also been amazing is this absolute revolution in our understanding the genetics of myelodysplastic syndromes. And as we understand more and more about these conditions, we're also slowly being able to identify therapies that target those genetic mutations, and we're hoping that will ultimately be the undoing of the MDS.

Caitlin

It's great to hear about these therapies, but what about clinical trials for a patient?

Dr. Sekeres

So, we consider clinical trials at any point in a person's diagnosis. And this is how I think about it: I only have so many tools in my toolbox to treat myelodysplastic syndromes. We have a limited number of drugs that have been approved by the FDA. If there's an opportunity to participate in a clinical trial, I'd love for one of my patients to consider it because I still have those FDA-approved tools that we can use later on in a diagnosis. So, we consider clinical trials for people with lower-risk, myelodysplastic syndromes, higher-risk MDS, and at any point during their therapy. Now, one thing, sometimes I've heard from patients, and I actually heard this from my own mother. My mother once said to me, "I never want to be a guinea pig on a trial." And I had to explain to her. First, I had to say, "Ma, I'm a clinical trialist. This is what I do for a living." But people sometimes forget that when you're on a clinical trial, at the very minimum, you're getting the standard of care. So, even someone for whom we're considering a clinical trial who has higher-risk myelodysplastic syndromes, we're always giving the standard of care, and then in addition to that, we're often giving another drug.

Caitlin

So, is there a cure?

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Dr. Sekeres

There is a cure for myelodysplastic syndromes and that cure is a bone marrow transplant, and sometimes people will call it a stem cell transplant or hematopoietic cell transplant. And when we perform that procedure, we give somebody chemotherapy and that opens up space in the bone marrow to then administer someone else's bone marrow. Actually, almost like we give a blood transfusion, it goes into, you know, one of the veins in the arm or in the chest, finds its way to the bone marrow, sets up shop and starts to grow, and hopefully grows a perfectly healthy new bone marrow.

Now, a bone marrow transplant has complications associated with it. So, it's a pretty serious procedure. We offer it to people who have higher-risk myelodysplastic syndromes. And that's because the risk of the myelodysplastic syndromes when somebody has higher-risk MDS – and by risk, I mean likelihood it could go into leukemia, or somebody would have shortened survival – is pretty high. So, if we're giving a bone marrow transplant, that risk may be lower than the risk of the MDS itself. On the other hand, somebody who has an incredibly low-risk myelodysplastic syndromes like you, the risk of the MDS is low, so giving a high-risk procedure like a bone marrow transplant doesn't make any sense.

Caitlin

Is there anything new or exciting on the horizon for MDS?

Dr. Sekeres

Actually, there's a lot that's to be excited about in myelodysplastic syndromes, we're increasingly getting better at understanding the biology of MDS in realizing it's not one diagnosis, it's hundreds of diagnoses with different genetic fingerprints defining each of those diagnoses. As we're understanding the genetics better, we're also developing drugs that can target those genetics. So, we have options for people with specific genetic mutations. Mutations like IDH-1 (isocitrate dehydrogenase 1) or IDH-2 (isocitrate dehydrogenase 2), FLT3 (fms-like tyrosine kinase 3). And all of these are a combination of letters and numbers that don't make any sense unless you actually stare at them every day like I do.

The other thing I'm really excited about and something I've been working on since I entered this field, is trying to combine drugs to get more of an effect than a single drug alone. There are three clinical trials right now that are in advanced stages that are looking at combinations of drugs for higher-risk myelodysplastic syndromes, and we're working on a number of drugs for lower-risk MDS.

Narrator

For tips to help you communicate with your healthcare team, including a list of suggested questions to ask your doctor, please visit The Leukemia & Lymphoma Society's website at [LLS.org](https://lls.org) to download and print our patient-friendly guides.

For more information about MDS and other blood cancers, please contact an Information Specialist at 1-800-955-4572 or visit us on the Web at: [LLS.org/InformationSpecialists](https://lls.org/InformationSpecialists).