

Speakers

Steven L. Allen, MD

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Jayshree Shah: I have a good, probably 25 minutes to kind of group my part real quick and then I want to have lunch and sit back, relax, maybe talk amongst each other and then the afternoon session again will be about you. I want to hear from you guys as far as your names, your diagnosis, what type of MDS you have and to ask questions and to learn from each other. I may not have all the answers and if I don't know the answer, I can always field it out to the Foundation and we have expert physicians that are part of the organization to answer them.

So, let me start over here. This is *Building Blocks of Hope* and this is created by Sandy Kurtin. She's a star nurse practitioner working in Arizona. If you look in front of you, the binders that were given to you that's a creation of all of our nurses and physicians combined together, all of our work. We have put different tabs inside the booklet, the binder, identifying different parts meaning the diagnosis. How do you identify somebody with MDS? What does it mean to have MDS? What does it entail with symptoms? What are treatment options? Those are some of the tabs and there was someone... a lot of questions that I heard for regarding iron overload. There's a whole section on that on it as well. So, feel free to read through it later on and browse later on about it. Feel free to ask any questions. I'm going to start with just kind of identifying about the management... Sorry, the meaning of *Building Blocks of Hope*. It's a global print and an online patient advocacy initiative providing a personal education program for patients and caregivers to prepare, participate and live with MDS. At the end of the day, we know what it takes in regards to us as providers and you as caregivers and patients to live with MDS and the way we know all of this and creating this model is believe it or not, we've done these patient forums for the last several years. All of the information that we've created in this binder is combination from your input. So, questions that you have asked, we put it in there because we've heard it repeatedly and we said this is important. So, we added it in and we want to share now with you. The colors, Sandy chose specific colors because she's from Arizona. So, she likes all the desert colors, the teals, the reds and the desert sand. That's why the color of the bind... the colors that you see on the binder, they're originally from Arizona area. This is a whole international nurse leadership board and we have included not just the United States, included around the world and we're talking about Europe, South America, Asia, all different areas and the reason we include it is because we want to integrate the entire world to be aware that this a big issue. This is not just something small. I'm awaiting Robin Roberts. You guys know Robin Roberts? I'm awaiting a book from her, a book or something in addition to what she went through with her developing MDS as a second malignancy. She initially developed breast cancer. Right? She received chemotherapy. A few years later, she developed MDS. Yeah. And so her story is a little bit different probably from what you guys are going to be sharing, but that's one story. It is not well known how many other people, famous people, may have had MDS. To me, everybody that has MDS is famous and I want you guys to share your story and I want to hear from Robin Roberts because ultimately we live in America, so celebrity sells and unfortunately, she needs to kind of up the par and she's going to eventually.

?: (inaudible 4:14) a book about that.

Jayshree Shah: There you go. So, she's in the works in writing her book, her story so that other people will know what MDS stands for.

MDS is new. It's new because it was not well known in regards to a name associated with it. We knew that there was a problem with patients who have anemia or low platelets or low white count. We then never identified it and called it a group calling MDS. Just recently over the last maybe 10 – 15 years they've identified other categories part of MDS, patients who have head link citterio block issues underneath the microscope. They looked at it and they said, "Oh, this is a special, different kind of anemia. Don't know what it is," but then they started grouping things together and find out and made it a group called MDS.

These are the topics that I'm going to be going over in general. I'm going to kind of breeze through it. I'm not going to be repeating what Dr. Allen already went through. I'm going to kind of highlight and just go through the generics of the different topics. If you have a specific question, again, hold those questions until after lunch and then we can talk about it. That whole hour is belonging to you. Okay?

Again, I'm going to pass this one along because that's what we're going to talk about. Let me just give you a quick overview aside from what Dr. Allen already mentioned and explained to you what MDS is. I love eating food. You do, too. I talk a lot of things and relate to food. Why? Because I can relate to it and understand it. I love gardening. I love gardening because I talk MDS with gardening and make association with it. I talk about the different seeds that we plant, tomatoes, peppers, jalapeños for me because I like spicy food. So, different seeds that we want to plant and grow, those are stem cells. I'm making an analogy here. Those stem cells if they're broken, the seeds are broken or they're discolored. They're not perfect. You know those packets that you get. They're like maybe 5 or 10 seeds in there. They don't look perfect they're not going to grow into the beautiful tomatoes and jalapeños that I want. Think of it that way. MDS in the packet they're broken. Not initially, but they get broken or they develop a little spot or something called mutations. Basically, it's a group of bone marrow cancers, a bunch of bone marrow cancers combined together and nonfunctioning. That garden it creates and develops into broken seeds that are not growing into fruition the tomatoes and jalapeños that I want ultimately creating MDS as a group. It's not one disease. It's a group of diseases originating in the bone marrow. The bone marrow is your garden. In the garden I want to plant both seeds. When I want to plant those seeds, what else happens within the garden? Lots of different weeds. They love coming along because you plant those good soil and all the nutrients and stuff. Those weeds come about also along with your plants. Those weeds represent scar tissue. It may represent blasts, bad, bad, cells. It could be anything. Things that don't belong in the garden pretty much and it overtakes it. When it overtakes it, it doesn't give room for the good seeds, the tomatoes and the jalapeños to grow ultimately. That's the end of product of MDS is. It's an overgrowth of weeds that does not allow the good fruition of the good stem cells to grow. The same thing when I mention those stem cells they become dysplastic. They don't look normal. They look abnormal. Those little seeds, they don't look normal.

So, this is your bone marrow. This is what everybody has in this room in your hip area right here. The liquid part, that's where we have all of our stem cells, all of us. When the physician or nurse

practitioner or a PA, whoever does the bone marrow, it wants to catch and capture a little part of the red marrow, the liquid part, but in addition to that, they also want to capture a little bone chip. Why? It has your information. It has Mike's information of who Mike is right now, not 20 years ago, right now. It wants to find out what's going on within his bone marrow. Those are the stem cells. Those are the seeds. The pathologists, the hematopathologist wants to look under the microscope and find out does Mike have any mutations? What does Mike have? The pathologist doesn't know what his CBC is. All he knows is that I've got a sample here of the liquid part and the bone marrow chip part, bone chip, and he looks in the microscope for any abnormalities, any less iron, does it look dysplastic, what else is going on? Is there scar tissue happening within the bone chip? All of those things are combined. In addition to that, the liquid part, a small part, a tube of it is sent over to a special laboratory for DNA analysis. It's called cytogenetic analysis. I want to find out... I hope you don't mind me using you as an example. Mike bone marrow, the liquid part, is sent over to the laboratory to find out what are his chromosomes. He has 23 from mom, 23 from dad. I want to find out those chromosomes. Are they mutated? Are they normal? What is going on with those chromosomes? If there are mutations, what do they look like? Does he have a monosomy 7? Does he have a trisomy 8? Does he have a 20? All of those numbers we found out there are certain mutations that people develop as a result develop in MDS or other diseases. This is your bone marrow. This is where your stem cells are. That's a stem cell going into... stem cell has a specific message already built in. Everybody's stem cell here. It already knows to say I'm going to grow today into a myeloid, red blood cell or I'm going to grow into a lymphoid. It has 2 different directions, but it already has a message. The myeloid stem cells, it can grow into a neutrophil, basophil, eosinophil, monocytes, platelets or red blood cells. Basically, what you guys are made of, what I'm made of. So, it already differentiates and tells you.

This stem cell, the patients who have MDS, sometimes extrinsic or intrinsic factors come into place and you're saying, "Jay, what does that mean?" Well, it means that maybe Jayshree was exposed to benzene or worked in a chemical factory for 25 years, 30 years and didn't have the proper inhalation equipment or work equipment to work around those kinds of chemicals. Maybe she got exposed to too much. Those are extrinsic factors causing defects in the normal hematopoiesis. So that when you keep on spraying some chemicals in your garden, right, to get those weeds out, who knows what those chemicals are doing to the soil. Maybe causing a little spotting of them stem cell seeds that we initially planted. Who knows? At the end of the day when that happens over time, not immediately, over time, it creates immature precursor cells causing the bone marrow not to function. Okay. That's the end result. Hence that's why you guys are here to learn about MDS, what you can do to make it better to live with MDS, what treatments/options are available. This is the whole panel. This is all included in your book. Okay? In your binder. If you want to. Don't write. Take your time to write anything down.

This is the whole workup and you're saying, "My God, Jay. That's a lot." It is. It takes a lot to go through and identify a patient with MDS because you don't want to make a wrong diagnosis. I've had one patient I can share a quick story for 30 seconds. She was a 35 year old African American woman that came into our office a consultation and we looked at her CBC and I went through the records beforehand and I looked at her records. No (inaudible 13:32). She was working. She was functioning. Doing everything right. Her CBC, I want to give you a quick layout. You guys are well aware and you're very knowledgeable about what a CBC parts that we

look at. The white blood cell, red blood cell and platelets. White blood cells helps you protect against infections, red blood cells your energy and platelets help you clot. So, I looked at those 3 numbers first, white blood cell 5.2 perfect. We want it between 4 and 10. Hemoglobin 5.1 ding, ding, ding, ding. That was a bad number. I didn't like that. Platelets, they were 125 pretty normal. The range is about 130 or higher to 400, so that was pretty normal. I thought to myself, "She only has red blood cell issue here." I looked to see if anybody did a bone marrow. No. She's coming in for a consultation to a hematologist to identify and find out what her problem was. So, we went through and we're like, "Maybe she has MDS." Maybe she's bleeding. First of all when anybody comes in with the low hemoglobin, that's a first rule out as a practitioner. Is the patient bleeding? She already had a colonoscopy. She had a whole endoscopy done. She had a stool collected. Everything was done in regards to the GI and that was negative. So, that was done. It was negative. So, we're like what's going on? She needs a bone marrow. We need to find out what's going on wither. In addition to doing the bone marrow, we also did iron saturation, iron levels, find out maybe she's iron deficient and maybe she has some kind thalassemia. Maybe she has some other kind disorder that we're missing. We did a B12. We did an EPO, hemolysis, all of these tests, blood work, in addition to the bone marrow. The bone marrow it takes about, you guys know, 4 to 5 days for the initial report and the cytogenetic takes about 10 days. While we're waiting, I got the labs back and of course we gave her a couple units of transfusion, too, because she was symptomatic. She was short of breath, feeling very tired, fatigue, the last couple weeks. Coming back, I looked at the lab results and I looked at her vitamin B12. She was vitamin B12 deficient. She didn't have MDS. You don't want to make a diagnosis on somebody wrong. It could happen. It can happen. Not to say happened to you, but you don't want to mess it up. It takes a really keen hematopathologist also to read the bone marrow. When I got the bone marrow results, normal hematopoiesis, normal platelets, normal neutrophils. I'm like looking at the report. Everything is normal. So, that I knew... that cleared it. She did not have MDS. She was vitamin B12 deficient. So knowing that part about the whole workup with MDS, it's very important that your oncologist, your physician does a thorough workup and make sure and identifies exactly what type of MDS you have. Knowing that part, there are different kinds. This is all included in your booklet. Feel free to browse through it. This gives you a nice classification breakdown of the different systems and different types of MDS.

So we've converted over from IPSS to IPSS revised. Dr. Allen did not include this in his slide deck. So, this is the newest version just to share with you and the newest because it came last year, going through in regards to the category of the cytogenetic risk group. So if you guys know where you fall into potentially, okay, if you have these mutations, the chromosome mutation, if you have them we're now able to kind of categorize them and identify which category does the patient fall into in estimating survival? Okay? Why do they do that? Because the numbers that they had initially used, a category, the types of patients they initially used did not match up with what was exactly happening. They still needed a more breakdown. They added more factors within to identify and break down the IPSS scoring system.

Again, risk categories that they included, the factors that I just talked about include cytogenetics, blasts, hemoglobin, platelets and ANC. ANC stands for Absolute Neutrophil Count. That number is basically your immune system. Okay? And it tells me when I look at a CBC, I don't look at the CBC alone, I look at the differential and find out do you have enough neutrophils? If you don't

have enough neutrophils, your immune system is not working. You may need help. You may need an antibiotic to protect you. You may need a growth factor to protect you. Okay?

This is survival information and the risk of leukemia transformation and, again, this is the newest version. This is all included in your handout in your binder. Feel free to browse through it later. This is the updated version, okay, in regards to survival.

And the facts about MDS. The average age of a diagnosis is 73. That's not to say we don't see patients in their 30s or 40s or 50s. We do. That's a average age. Okay? MDS still remains an incurable malignancy for the majority of patients. Allogeneic transplant is the only cure. The leading cause of death itself is MDS. Risk stratified treatment strategies are key to an optimal therapeutic options. Individualized treatment. It's very important. Every patient that is here, every patient meaning... Can I just get a raise of hands real quick? Patients. All of you guys do not have the same type of MDS. Every patient that has MDS, you have a little bit of variability and that's what makes you special because it's in individualized treatment. Yes, we can categorize and say you have RAB, RARS, but there may be something extra special about you that makes you just you with MDS and that's what makes so special because your oncologist has to identify that special link about you to figure out a treatment plan for you. For that patient that asked the question, "Oh, am I eligible to get cyclosporine now because I'm hypocellular questionable aplastic, now MDS." Again, that patient's different than that patient. It could be that it may work for that patient.

There's a whole bunch of factors associated with individualized treatment. We look at performance status, comorbidities, identifying the IPSS scoring system, primary versus secondary MDS. There's lots of patients now that we're seeing that potentially received treatment for other cancers, 10 or 15 years later developed MDS and I'm talking breast cancer, I'm talking about prostate cancer because they may have gotten radiation or chemo or something related and now developed it. Cytogenetic status and lifestyle. We look at all of those factors and then we combine it and we try to figure out what would best... what would be the best treatment for you. Is transplant an option? Current treatments. Dr. Allen went through a whole bunch of all of these. I'm not going to go into detail. Revlimid, Vidaza, Dacogen, chemotherapy, transplant, investigational drugs. Again, a whole slew of different treatments, but I'll be honest with you. These treatments this little compared to what is available for other types of cancer. We have a long ways to go. We have a long ways to go.

These are the nice... This is a nice slide in regards to mechanism of action and therapies under investigation. You may potentially be participating in one of these trials or know of somebody that is running a trial. Some of them may have even closed like the Onconova that Dr. Allen mentioned. It just closed in regards to accruing enough patients and the data. This is important in case anybody is interested in participating in a clinical trial and want to know more about it. Key principles of therapies in MDS. Again, allogeneic transplant remains the only potential cure. Age alone should not exclude active therapies. That's a key statement. That's a bold statement. You know, I've had patients come into our office for a consultation and the only thing that have been offered to them is supportive care. It's not the case. At least we have a few different options available to improve their quality of life and it's very helpful to know that we have something available versus nothing which we didn't about seven to eight years ago. All active therapies of

MDS require a time to work. That's another key statement. With MDS, we know that it takes awhile to take those weeds out. If you spray it once, right, in your garden, the weed whacker or whatever medication or chemical, whatever in the garden, it's not going to get rid of it immediately. It may take 1 week here, 1 week there. The same concept. You need to keep on giving the medication continuously and not stop. I've also had patients that have come into our office that have received Vidaza for... or Dacogen whichever hypomethylating agents for six months and the oncologist decided to stop because it worked and the counts normalized and said, "Oh, six months. You responded. Good. You keep going. No more treatment." No. You want to keep going. Why? Because, again, MDS can come back. It can come back potentially with a vengeance and developing into AML.

Proactive management of side effects in early phases of treatment are key to obtaining a best response. Again, we can only learn from you as patients in letting us know what's happening to you. What can we make... what can we do to make your quality of life better at home? We only see you for 15 – 20 minutes if that in the office and we ask the necessary questions to figure out a care plan for home. So, it's important that you write down what symptoms you've had for the week that I did not see you. "Jay, you know what? I didn't do much," and I'm going to say, "Well, what did you do? Did you go to church because I know that you enjoy going to church. Did you participate in your bridging club? What did you do? Did you go to the garden? Did you do anything? Any activity? What over thing did you do," so I can feel out what I need to do for a plan wise to help you make it better.

Just a nice overview about treatment, why it takes time to... why time is required and understanding with management of patients how get treatment with MDS, for MDS. Blood counts drop as MDS progresses and normal blood cells are crowded out which I mentioned, basically the weeds kind of going through the garden and wants to overtake it. We have blast cells over here and what happens is it's a big dip. When you first get... Is there anybody over here received Vidaza or Dacogen. Raise their hands. Yes? Okay. Vidaza. Okay. So when people receive those hypomethylating agents and it takes awhile if you (inaudible 26:22) back when you first got it, you were probably getting transfusions left and right, you're feeling tired and fatigue. That's the initial because think about it. If you have your garden 80 percent completely packed with weeds and only 20 percent with just plants that are growing, it takes awhile to get rid of that 80 percent. Right? It's the same concept. Just the same concept because you keep on needing to hit the garden with enough medicine to get those weeds out.

The bone marrow begins to recover allowing it to make healthy blood cells, blood cells counts rise in symptoms of MDS should improve. Patients can be weaned from supportive care as a robust response sets in. Again, we're trying to get rid of the blast cells and we're making normal white blood cells and good platelets. Early toxicities may be difficult and are discouraging for the patient. My patients who get any kind of hypomethylating agent when they first diagnose with MDS, I tell them you got to be patient. It's a contract. The first time I meet them I tell them this is a contract. It's a commitment for the first four to six months it's a commitment and letting you know it's going to be tough, but my role is to keep you safe, improve your quality of life over time, but it's work in progress. It may involve a lot more visits initially, okay, but the end result we want you to have and maintain a good quality of life and function and live.

This, again, working together for the best response. It takes time to get that response.

This is a nice just a chart, a bar graph, treillage, response following 4 cycles of Azacitidine. Again, it takes awhile before the patients start responding. That's what this chart is basically breaking it down to and patient response over 10 years of Lenalidomide treatment. Lenalidomide is, again, Revlimid. This is Sandy's patient, the nurse practitioner that works in Arizona. She wanted to share this with you to letting you know that patients can start off with poor numbers and then eventually maintain and improve over time. Stable numbers, stable quality of life over time when they improve is a good thing. I think we, as humans, want a response. We want a robust response. We want a cure response. We want a remission response immediately. With MDS it does take time. For this patient, again, being on Revlimid, they maintained and done really well while they have been on Revlimid. This is just a nice showing of a good response.

So what can you do in staying healthy, but have a balanced diet. You know, you may not participate or go to a big cancer center that I kind of work at. You may be going to a communitative physician or oncologist. What I tell patients or caregivers is pick up the phone and look in the Yellow Pages or Google it and find the biggest cancer center and tell them, "I'm not a patient there, but I need information." Guess what? They'll hook you up with a dietician, a social worker, whatever you need because believe it or not I get phone calls from all different areas saying, "Jay, I need advice," or, "I need this," and I try... my job is to link resources that are available to what patient is asking or the caregivers are asking. Okay. Again, use MDS as a middle party in helping you get whatever resources you need.

Daily activities and exercise. Patients often ask me that especially MDS patients. "Jay, can I go do aerobics?" I'm going to say, "Not probably with a hemoglobin of 7. I don't want you to pass out, but you can do walking." Walking. A simple thing like getting up and waking. Okay. A simple thing like that. If you feel like carrying a 1 pounds weight doing it, that's fine. Carry a cell phone. Safety comes first. Talk with your physician or practitioner about it before you start doing any kind of activity or exercise.

Avoiding infections. Don't put yourself in a bubble. I want you to live. Okay. Immediately when patients are diagnosed, they like, "Jay, can I go outside? Can I eat this? Can I eat fresh fruit? Can I eat vegetables? Salads?" Yes, yes, yes. There's no restrictions. Common sense stuff. You're not going to pick it from the garden, the beets or potatoes and start eating or just washing it and eating it. You want to peel it, cook it. Right? Common sense stuff.

Avoid bleeding. Again, know your numbers. Get educated. That's why you picked up the binder. That's why we gave it to you. Education is your key and understanding your disease. Okay.

Continuing to enjoy things you love. Live. If it makes you happy to go and take pictures or do photography or travel, try it. Small trips. Take weekend trips. Whatever makes you happy. Right?

Get enough rest. Sleep is huge. Did you know when you sleep you regenerate all your stem cells and your energy cells and your white blood cells? If you need a nap, go ahead and take it. It's okay. It's okay.

Ask for help when needed. Again, take advantage of the available resources. This is all online. If anybody wants to go on the MDS Foundation website you can click on different avenues on the website to find more information. Be an active participant in building hope. Okay. That's why you guys are here because you're sharing your stories and other people get motivated and saying, "That lady's doing it. Why can't I?" Yes you can.

And becoming a partner in your care, building your MDS individualized plan. Thank you. That's all I want to say. We're going to stop here and good timing. Think of questions. We're going to introduce ourselves because I want to know who everybody is here and you'll feel people. I actually met my patient that I've taken care of for a long time and she's come and... yes. So, it's a pleasure seeing here after a long time and lunch should be ready, I think, outside through the door. Thank you.