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Denise McAllister: Good morning, everyone. I understand that everyone is here and registered. So, we will go ahead and get started.

?: If there's any questions, it's asked that you could repeat the question in your answers so we can hear it on the recording.

Denise McAllister: Sure. Thank you very much. Okay. I have instructions. Any questions, I need to repeat it. My name is Denise McAllister and I'm an oncology nurse practitioner working out of Tampa, Florida. I have worked with patients with Myelodysplastic Syndrome since about 1989. So, it is a pleasure for me to be here in St. Louis today and as well as representing the MDS Foundation, which is an organization that really does great work for folks with Myelodysplastic Syndrome.

I'm going to introduce to you a program that is now available through the MDS Foundation and you currently have a binder that represents this program. It's called *The Building Blocks of Hope – A Patient and Caregiver Guide for Living with Myelodysplastic Syndrome*. This was actually the vision of Sandra Curtain who is a nurse practitioner working out of Tucson, Arizona. She really is recognized as an oncology nursing leader when it comes to MDS. The thought that was put in to this program really makes this the most comprehensive go-to book for MDS knowledge that I have seen in my career that I truly think exists today. So, I'm going to go through this slide deck introducing this program to you which you definitely have access to.

First of all, the MDS program has... excuse me, the MDS Foundation has an International Nursing Leadership Board and this is what I am a part of. It's national as well as international. When we look at the content that's housed in that book that you hold and is also available on the MDS website, it gives you an understanding of what is myelodysplasia, how is it diagnosed, what are treatment options, what are common side effects associated with treatment and how can those be better managed, what new treatments are on the horizon to treat patients with myelodysplasia, what are the consequences of blood transfusions, what is the role of iron chelation therapy and how to select a bone marrow transplant center and it also gives some tips on how to keep healthy with the diagnosis of myelodysplasia. So, this *Building Blocks of Hope*, it's in print as well as online incorporated in the online version, there's video clips that you can log into to give you a better understanding, but, again, it looks at the disease itself. What is someone's scoring system that helps us identify what patients' risks are when it comes to myelodysplasia? There's also a section for questions to ask such as schedule, possible side effects, how to manage those side effects as well as looking at lifestyle. There's also a section on asking for help and that can absolutely be one of the hardest things for people to do. One thing that I have learned very early on when it comes to cancer care is that there's a lot of people who want to help whether it's family members or it's neighbors, but sometimes people don't know

how to offer that help so really what people need is an assignment. Even it may be a neighbor bringing out the garbage can to the side of the road on garbage days. That makes people feel useful and that they're contributing to someone's daily wellbeing just by having the ability to do something no matter how small it may seem. So, I would definitely encourage you to consider reaching out to others when needed.

This tool also gives the ability to empower patients and caregivers to become a partner in their own journey with myelodysplasia with their healthcare team and it also encourages folks to track their progress by recognizing what their prognostic score is, what are their laboratory results and how does that equate to their present state of myelodysplasia.

So, what is MDS? Certainly what we know is it really is one... it starts with one cell and that one cell can go on to multiply and divide and create problems. With that one cell though, myelodysplasia is what we call a very heterogenous disease that it can look very different. So, someone may have or people can have perhaps the same risk category, but their disease may have very different features about it.

So, what happens? The cells in the bone marrow are abnormal. They are misshapen, they do not function normally. So, someone, for example, who may suffer from anemia because those red blood cells are oddly shaped, someone who may have a hemoglobin of 10, for example, may feel like their hemoglobin is seven or eight. They may be very fatigued, very short of breath because those cells do not function normally. Someone who has dysplasia in their white blood cell line, for example, may not have good infection fighting ability just because those cells do not function as they should. When we talk about cytopenias, we're talking about low blood counts and those are the counts that we measure in your CBC every day that you also have access to. You're looking at that as well. Certainly what we know about myelodysplasia is that it carries a risk of transformation to acute leukemia and the higher someone's prognostic score is the higher the risk for developing acute myelogenous leukemia. So in general, the bone marrow function is not normal. With the healthy marrow, which rests in the center of our long bones, is the liquid portion. That one stem cell goes on to become whatever the body needs it to. It can become a white blood cell, it can become a red blood cell or it can become a platelet. So in a healthy, normal bone marrow those cells are produced in normal number, they also have a normal shape and they also function as they should to protect the body with white blood cells protecting against infection or helping get rid of infections, red blood cells carrying oxygen to our tissues and platelets which control bleeding.

When we look at myelodysplasia, for example, the bone marrow absolutely does not function normally that something goes very wrong with that stem cell and, of course, it goes on to make other abnormal cells. Sometimes people may have dysplasia just in one cell line like their red blood cells, for example. Some people may have dysplasia in two cell lines like their white blood cells and their red blood cells. Some people may have dysplasia in all three. What we also recognize is that about 90 percent of folks with myelodysplasia when we do someone's bone

marrow biopsy, it comes back as though there's a lot of activity going on, but when we're looking at someone's CBC, it just doesn't equate because blood counts can be suppressed or they can be low. So, we recognize that there's a disconnect in what's truly happening in the bone marrow as with that biopsy as far as the volume of cells, but it doesn't equate that way onto someone's CBC and that's because a lot of those cells are dying off prematurely. As someone... just to go back, as someone is transforming into acute myelogenous leukemia or have high risk myelodysplasia, it's these immature cells that are present that are taking up space and crowding out our good cells.

So, how do we diagnose it? The way to diagnose it is through that bone marrow biopsy and aspirate and, of course, looking at someone's CBC can give us a hint that there's an abnormality, but the best way to diagnose is through a bone marrow biopsy and doing special studies like cytogenetics, FISH. When someone does have an abnormal CBC, it is important, though, as healthcare providers that we look at other causes. Why someone is anemic? Do they have iron deficiency, for example? Are they deficient in B12? Is their own body destroying their own red blood cells? Does someone perhaps have an abnormal thyroid function that could be contributing to that? Does someone have sluggish kidneys where their kidney functioning is not the best? That can create anemia. Our kidneys secrete a hormone known as erythropoietin and that sends a signal to stimulate more red blood cell production. So in myelodysplastic care, to get a baseline erythropoietin level is important because if someone does have a low erythropoietin level and a low transfusion burden, we know those are the folks who are going to be the best responders to erythropoietin. I heard someone talking about Procrit earlier and that's exactly the drug that I am referring to.

Denise McAllister: Yes, ma'am.

Q1: We had a bone marrow biopsy (inaudible 11:59). Is that not definitely (inaudible 12:01). Would that be in the initial test or are you suggesting to give you additional test first?

Denise McAllister: The additional test is really a standard of care. So, those are done anyway. Those tests though do not diagnose myelodysplasia, but they'll help look for another cause as to why someone may be having anemia as an example, but the way to diagnose myelodysplasia is through the bone marrow biopsy, but we also want to exclude other abnormalities such as iron deficiency anemia or B12 deficiency, etc. That's a good question. Thank you.

I'm going to go through this, but I recognize that we have a physician here who's going to be speaking with us in just a few moments. So, I'll spend... I'll go over this very briefly, but early on in MDS care, we had the French American British Classification and then as time has gone along and we have grown to know more about myelodysplasia, there have been updates to the classification system to help clinicians and everyone better define myelodysplasia and look at specific characteristics of the disease and that can help clinicians guide therapy choices as well. Then we have the International Prognostic Scoring System and this helps us identify survival in

folks or what is their risk for transforming to acute myelogenous leukemia. So, it can help guide therapy, but what's important to recognize is these scoring systems, it's based on data without treatment. Also what you'll find in *The Building Blocks of Hope* is detailed information about the scoring systems and also how to link on to that.

So, what do we know for sure about myelodysplasia? The average of diagnosis is 73. So, it does tend to be a diagnosis in folks of the older adult. It remains incurable. What we also recognize is that allogeneic transplant can be the best opportunity for cure and I heard someone talking earlier, as well, about the leading cause of death is the disease itself. Infections can be huge. Bleeding can also be a problem as well as transformation to acute myelogenous leukemia, but we definitely have come a long way when it comes to this disease and especially with the amount of research that has occurred that has gotten us where we are today. When I first started taking care of folks with myelodysplasia back in 1989, we did not have any therapies at all to change the history or the natural history of this disease and today we do. So now when we look at folks that who actually needs treatment, it's those who are symptomatic with their myelodysplasia such as folks who are blood product dependent. Those who perhaps have some neutropenia or low white blood cell count that puts them at risk for infections. Do they have an increasing number of those immature cells or are there blasts in their bone marrow and, of course, those folks with high risk disease. So when healthcare providers are looking at how to make the best decisions for treatment, certainly what's important to us is how people function every day, how they live every day and how they're able to take care of themselves. I saw a lady yesterday, as an example, 76 years old and when I look at her and I see how well she gets on and off the exam table and talking about traveling here and traveling there, I looked at her and I said, "I forget that you're 76 years old," because she is not... she doesn't have the performance of someone who you would think really and truly is 76. So, truly how someone functions every day.

Comorbidities. Today on the average the older adult has about three or more comorbid conditions and, for example, that could be a thyroid problem, a blood pressure problem, sluggish kidneys as we talked about among others. Also, what is their International Prognostic Score? Is this an MDS that just occurred out of nowhere or is it an MDS that occurred as a result of perhaps prior therapies that someone has received? What are their risk features when it comes to looking at their DNA and deletion 5Q really is an... it's the most common cytogenetic abnormality that exists and, of course, we have a therapy today known as Lenalidomide or Revlimid that targets that specific abnormality and that can be the chromosome abnormality by itself or in combination with other abnormalities and, of course, lifestyle and patient preferences are important when it comes to how care providers defining treatment.

So...

Q2: Did you say Thalidomide?

Denise McAllister: I said Revlimid or Lenalidomide and you ask a very good question about Thalidomide and Thalidomide was certainly a drug that we had used early on that did make some difference in peoples' transfusion improvement, but it really didn't change the true history of the disease like what we've seen with its analog Lenalidomide, a newer generation, Thalidomide that has really made a tremendous strides.

So, whether you're being treated a community setting or you're being treated in an academic setting, supportive care is important. Support people along with transfusion and growth factors as they need it. When we look at current FDA approved medicines, there's Revlimid or Lenalidomide. Vidaza and Dacogen, those two agents are FDA approved in all subtypes of myelodysplasia and then, of course, when folks need out and out chemotherapeutic agents, those are certainly available and that's what we used early on. Bone marrow transplant or stem cell transplant can be an option as well as clinical trial and this just gives a small hint of the activity that's going on behind the scenes in the laboratory as well as in the clinic to try to improve up on the treatment strategies that we have here today and if you notice this is dated 2012 and we're in the year of 2014. So, needless to say that list can look must different today as far as length if it were updated.

So, key principles. As mentioned earlier, allogeneic transplant is the best option for cure and today we're getting away from age really. It's more about performance status, comorbid conditions in defining therapies. Therapies can be slow to work, so patience is key. So, just please keep that in mind that some therapies can take months really before you see an improvement and we'll talk more about that. What's very routine in MDS care is we know that we're starting out with blood counts not being their best and when people receive treatment, those blood counts can get worse before they get better and that really is an expectation so to speak that we have and that we anticipate that.

So before treatment begins, as stated that bone marrow doesn't function normally and blood counts can be very much suppressed before treatment even starts and remember it may be just a hemoglobin that's suppressed, it may be a white blood cell count in combination with that and/or platelets. So, blood counts are abnormal and that's what prompts people to need treatment. With therapy, as a result of treatment, the blood counts dip further and the goal is that they will populate with more normal cells. Something, too, that's important to recognize is that as blood counts drop you have a healthcare team that's really kind of down in this hole or this ravine with you supporting you along with blood product transfusion, growth factors, if people know their antimicrobials. Whatever it is to help pull people out of that slump with their labs and allow in hopes that their bone marrow is going to start to produce normal cells again, but if you notice the graft up here, this clearly depicts where someone started and as a result of treatment their white blood cell count and their neutrophil count or infection fighting ability plummeted, but then with time it came back up to a more normal range.

When blood counts are low, people already are frightened and you may see that yourselves when looking at your own CBC when blood counts aren't normal. You want to turn this around and with treatment people can get discouraged or feel that treatment's not working or the treatment's too toxic and they're not going to be able to continue. Patience is key in partnering with your healthcare team to get through that downside when blood counts are not their best. So again, blood counts... the bone marrow can populate with more normal cells and get rid of those dysplastic features as much as possible.

Too, it's not uncommon that with treatment even blood counts, people may develop a new normal, but you see here hemoglobin, for example, this is platelets and this blue line here is white blood cells. You see that with Azacitidine or Vidaza, this is after four cycles of treatment. You see this up and down, up and down and then finally you see where someone's blood count start to recover and to higher than what they were prior to starting treatment. So, that definitely indicates a response, but remember patience is key and do not get discouraged if you don't see that response within one or two cycles. It can take four to six months. I've seen patients respond after a year with Azacitidine, for example. This is someone's response after 10 years of receiving Lenalidomide and you see where they started and now you see that their blood counts are where they no longer require transfusions, they're not at risk for infections and they're not at risk for bleeding.

So, how to stay healthy. In your booklet there's some great tips of eating a good diet. Activity or exercise is important. Someone once told me that motion is lotion. It's good for the joints, good for the bones and it also helps counteract fatigue. So, that piece is important. Avoid infections when you can. Use good hand washing. Stay away from people who you know are sick and that antibacterial gel can also be helpful and when platelet count is low that puts folks at risk for bleeding. It's important to do everything you can to avoid bleeding, but at the same time in this period throughout your life where things are not normal and perhaps you're having to use more precautions than usual. As a healthcare provider, we always want people to live the best life that they can each day and that's what we certainly encourage of you. Get rest when you need it and certainly take advantage of available resources such as *The Building Blocks of Hope* and reach out to neighbors and other family members who really want to help, but perhaps don't know what to do.

There's also "Healthy Body Healthy Mind" which is the longest running holistic program that has been on public television and there is also a segment on myelodysplasia and I think you may have the disc in your notebook, so that's something that you can also take advantage of. Becoming a partner in your own care. You can track your labs. There's trackers available through the MDS Foundation. They're also in your booklet. Keep up with the medications that you're taking. Make a list. Take it to your doctors' appointments each time, so that can be updated with ease. This tool that you have in front of you, it's very interactive. Again, you have the print version. There's online version. There's embedded videos hearing from patients as well as caregivers and I encourage you to really use that as your go-to source for information. It's the



most comprehensive tool that I have seen in my career when it comes to managing side effects of the disease as well as the treatment.

You can create your own MDS plan and as mentioned, there's tools for tracking your progress. There's links that you can gain more access to and, of course, a wonderful resource for folks with myelodysplasia is the MDS Foundation and, of course, Audrey who's sitting out there now.

The Building Blocks of Hope when it comes to materials, Understanding MDS, Seeking Treatment, Quick Tips for Managing Symptoms. Also a segment on Iron Overload, a segment on developing and MDS plan and also a very detailed section on the MDS Foundation and how they can help.

That is the introduction to *The Building Blocks of Hope* and I hope that you will find that resource as useful as what I have in my career and I'm going to stop here and introduce our keynote speaker.

Q3: I have a question. When you (inaudible 27:41) (END OF AUDIO)