Speakers:
Larry D. Cripe, MD
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**Larry D. Cripe, MD:** And so all that elaborate machinery is trying to do that. So as many of you know, really the first sign of MDS is when one of those blood counts is abnormal or there's something abnormal about the appearance of those cells and one of the first things we always do and this may come up is really how do we decide it is MDS versus something else versus something else that's injuring the bone marrow and there are many people… I was just before I came into work I was… or came here I was dictating a chart on a lady I had seen that I don't know yet. I know her bone marrow has failed, but we don't quite know yet what is causing that.

MDS is a very specific disease or group of diseases that is caused by genetic damage to what's called the stem cell. So, you can think about the stem as the seeds of the bone marrow that occasionally provide more cells. So, everything's being produced. There's a lot of things that can affect the stem cell behavior, but MDS is really something intrinsic to this cell, has damaged the cell's DNA and so it can no longer do that.

So, that's one potential area we may want to talk a little bit about is how do you really know it's MDS? What's the implication of that, but once we're pretty sure somebody has MDS, then at least in my opinion what we're trying to do is understand what the implications to that person's life in that moment or that near future and then what's in the long term future and I don't know that there's a way to really language this better than this, but I think it's pretty good language and so basically we say so if you think about what the bone marrow function is and the blood cells are we talk about risk. Right? We talk about what is the risk that the bone marrow will not produce enough cells and somebody's going to need transfusions or not produce enough white cells and somebody's going to have infections or not need enough platelets, so somebody's going to have problems with bleeding and then also it's axiom of human health that once a tissue has sustained one genetic damage, it's susceptible to additional genetic damage and for MDS that is manifested by this proclivity in some people for the disease to progress to a disease called acute myeloid leukemia and so we think about the risk. So, we think about what's the immediate implication of the disease and then what's the risk of the disease.

Now, I imagine many of you in this room are far more sophisticated than I am about some of the risk categories because I'm more of a lumper than a splitter. So, I tend to encourage people to think about there are people who have higher risk disease and there are people who have lower risk disease. You could get up to seven or eight risk categories, but I tend to think that that's… it's just getting harder and harder to distinguish between the difference, but the main difference is from my standpoint is what are the goals of treatment, what are the goals of the care we're trying to provide and what makes sense in terms of what's likely to happen with that individual with some form of treatment or not. Okay.

One of the biggest things I think I do is as a blood cancer specialist is try to make sure that I don't do something too soon or recommend something too soon because everything we do potentially has risks and can really muck up something. So to me, the risk concept is very important so… and I think you probably all are aware of this, but from a medical standpoint we sort of think well, if somebody's at high risk for something bad happening from the disease, it may make more sense to encourage them to do something that puts them at risk because what you're trying to do is you're trying to gain for them. So, you're always trying to look at where is my risk and where is my benefit. So that I think will be as I remember the last time I did that I think that's really the biggest chunk of stuff we may want to talk about.

And then a final one which I'm happy to go to but I'm always nervous about it is what's on the horizon. So one of the reasons I probably moved away from doing more drug development than I do right now is I'm not inherently an enthusiastic person. I'm inherently… I probably should have been from the State of Missouri because I always like to see the evidence first. So, I don't want to be Debbie Downer on this Saturday morning. So, I know there's a lot of things out there. I truly believe what we know about this disease now compared to what we knew about 10 years ago is dramatically different and I believe that someday we're going to be able to make more of a difference, but I think right now for us struggling with the illness and its implication, I tend to say well, let's work on what we know about as opposed to think about what will come three to five years from now, but I'm happy to entertain any questions.

So, without further ado, I'm hoping at least one or two of you are impatiently waiting to ask a question because we're going to need to get this going. So, I'm going to stop and entertain any questions. Yes, sir?

**Q1:** In the context of what we know now, it's a genetic related disease. Are there any… Do you have any tests that can distinguish different types or degrees of the disease?

**Larry D. Cripe, MD:** Yes, but let me clarify something that I think is difficult for us we need to keep grasp of. It's genetic within the cells of the bone marrow.

**Q1:** It can be spontaneous.

**Larry D. Cripe, MD:** Well, no. I'm more saying it's… So, sometimes when people say it's genetic like hemophilia is genetic and that means what we say when we say that's genetic we say it's transmitted from generation to generation. Most people who have MDS, there is not that familial genetic damage. So, the way I think about it is we are all subject to think in the environment that induce genetic damage and thankfully, almost always our cells are able to say okay, I have genetic damage and the cell asks itself a question. Can I fix it or not? And if it can fix it, it fixes it and everything's fine. If it can't fix it, the cells are really programmed to just die. So what happens something very early on, a stem cell in the bone marrow is damaged genetically

and it is not able to die. So, it propagates that genetic damage. Am I answering your question so far?

**Q1:** Yes, yes.

**Larry D. Cripe, MD:** So, and then as I said earlier it's an axiom of cells that once it's learned to tolerate one set of genetic damage, it can tolerate more. So then what you see is sort of a cascade of further genetic damage and one of the things that we used to think when I was training is that a cell became damaged and its progeny were all identical and that's not true. So, now I'll get to your question. So, 1) is that we like to look for evidence of genetic damage in order to prove that it's MDS because there are diseases of the immune system. There's drug associated bone marrow failure that we want to make sure we're not missing. So, the one that everybody does is what's called the metaphase cytogenetics. So, if you look at the actual chromosomes themselves under the microscope. Then there's something called FISH which is a more sophisticated way to look for genetic or structural damage of the chromosomes and then there's molecular studies that can actually narrow down on specific genes and look for abnormalities. So, you say I want to know gene X, is it normal or abnormal and now there are techniques where you can actually essentially scan the whole genetic material of the cells. I think it is fair to say as a topic of legitimate debate about what we should be doing uniformly. So, it goes like this. So if somebody has mild bone marrow failure, it's probably not worthwhile doing all that because 1) they're probably likely to do okay for a number of years and you're not likely to want to do some aggressive form of treatment. On the other hand if somebody, for example, this lady I saw the other day, she really has virtually no platelets, no red cells without transfusions. It may be worthwhile to do that to try to prove once and for all is it a genetic disorder or an acquired genetic disorder of the bone marrow. Now, there are colleagues of mine who are very smart and very compassionate people who feel we should do it for everybody and we should integrate it into our decisions and our recommendations. I'm more cautious than that because I don't think we have enough information yet to be able to say based upon this genetic damage, we should think about your future differently or we should be able to do treatment differently. Is that…?

**Q1:** Very good. Yes.

**Larry D. Cripe, MD:** Okay. So, let me just say for… I will say that there is this thing out there just in case your doctors talk to you about it. There's something called TET2 and there's a group of drugs called the hypomethylating agents and there does seem to be some predictive value in terms of who's likely to respond to hypomethylating agents. So, that's definitely one of the things people are very excited about and that's an example of what we'd like to get to. We'd like to be able to do this testing and be able to say you have the disease and with this genetic profile we should give you these drugs and move on, but we're just not there yet. Thank you very much for that question.

What else? Who else? Don't be bashful. We all have questions.

**Q2:** How do people do on Vidaza? What's generally their experience?

**Larry D. Cripe, MD:** So, people… So, the first American trial of Vidaza had a companion trial where they measured peoples' quality of life who were on the drug. Now, these individuals had a wide range of diagnoses within MDS, a wide range of risk categories. So, it's not where we now use Vidaza which is we use that mainly in people with higher risk MDS, but in that study it actually showed people on Vidaza had a better… reported a better quality of life than people who were not on Vidaza. So, now that's populations. I'm looking at Jean because she's advanced practice nurse and there's always a slightly different perspective. So, feel free to jump in anytime. So, I think a doctor could say to the people I think in general you'll do better with it than you won't, but there's a couple of things I'd share with people before I started. One is almost always your transfusion needs will increase. So, we often do it for people who are needing red blood cell transfusions. Almost always a need for transfusions will increase in that first one month or so. I don't know whether it's the drug itself or whether what we do to prevent nausea, but many people that I take care of develop constipation. So, we always encourage to get that under control before you stop it. Let me think and then the way I explain it to people I think it's a bit like agreeing to walk across thin ice. Most of the time as long as the ice holds you'll be okay, but you do have to be prepared for the idea that you will get rare complications that are more associated with how we think about chemotherapy – mouth sores, the blood counts can sometimes go much lower than we expect on average and there's an infection risk or a need to be hospitalized to treat infections. There can be damage to the kidney or the liver. So, does that analogy make sense? Most people get across it okay, but you have to sort of guard yourself for the idea that you are exposing yourself to some risk and until you see how your bone marrow responds, so what we're always… With chemotherapy for bone marrow disorders, we're sort of thinking about okay, so we're going to make things worse in the short term in hopes that when it recovers, you'll be better off than you started before, but during that period of time it's hard to know.

**Q2:** The reason I ask is I'm on Revlimid now and have been for year, started at 5 milligrams. The doctor had increased it 10 and immediately took me off of it. I'm taking 7 ½ now and he said that's too much.

**Larry D. Cripe, MD:** Do you know why he took you off of it or she?

**Q2:** The red blood cell count wasn't going up enough and platelets and white cells were down, but he said the end of this year he's going to make a decision and he mentioned Vidaza and I was just trying to get some… I've read things, but I wondered what the real world is you've told me.

**Larry D. Cripe, MD:** So, may I put my nose in one more second?

**Q2:** Sure.

**Larry D. Cripe, MD:** So, I think one thing I would… I encourage everybody whether it's my family, friends, myself or my patients. Make sure you know what the decision… why that decision is being made. So, I have two suggestions I think that… your doctor will appreciate this. It's sort of a sentence. If I start Vidaza, I will experience… and make sure that your doctor and you are on the same page about what you're really trying to do because this is in my opinion the most important thing about these decisions is I may as a doctor think a response is worth treatment, but if I explain it to you you may say well that's not my problem with my MDS and if you do that that's not going to make… So, one, and then two, to sort of do ask what is the best case scenario and what is the worst case and then you will get those two things. You'll get the idea that your quality of life will improve, you'll need less transfusions, you'll feel better, but there's also the worst case where you may end up in the hospital with mouth sores, infections and needing more transfusions. Does that make sense? So, make sure that you agree with your doctor that the goal. So, what I try to do with everybody is I try to list the goals. So, what are we trying to do and then to make sure that I know what their goals are and make sure that we share a goal. So, it's hard to explain, but I'm looking at it as a disease and I know that there's people attached to that disease and so I'm trying to be sensitive but you should look at it a person with the disease, I think.

**Q2:** He's open and he tells me what's going on. Just one comment when we came in you said something about the starting of medication. He held off as long as he could. I was on a wait and watch for over three years and he said he didn't want to start too soon because there are just so many drugs and if you start too soon you go off the other end with nothing. I mean, there's a point of which there're no drugs.

**Larry D. Cripe, MD:** Well, you shouldn't start before there's some benefit to starting.

**Q2:** No. He waited.

**Larry D. Cripe, MD:** I think that concept of delaying using a drug because you want drugs available is very controversial is all I would say.

**Q2:** At the point he said it, I could read the CBC by then. Things were getting ugly. I know they weren't at the really ugly point.

**Larry D. Cripe, MD:** Right. I agree. Yes, sir.

**Q3:** I have been on Vidaza now for nine months and I'm at the (inaudible 18:27) amount and I guess I'm doing okay. A year ago September or a year ago August I went to give blood at the blood center where I've given over nine gallons and they saw something strange. September I wound up with Dr. Birhiray and he looked at my tests and said, "If you don't start chemo tomorrow, you'll be lucky if you're alive at Christmas," three months and so I'm no dummy. I

started chemo the next day. The first six months he gave me Dacogen and was on that and at the end of six months which was nine months ago now he put me on Vidaza. Constantly talks about my quality of life. The day he told me that I maybe had three months to live, I felt perfectly fine. There's nothing wrong with me. I still feel that way today. I still have plenty of pep. I still have plenty of energy. I have not had any side effects from any of the chemotherapy I have. I get seven days in a row and I get three weeks off, seven days in a row, three weeks off. I've now had 93 doses of chemo and I still have hair and so and I still feel fine and so he's constantly talking of quality of life and right now the Vidaza seems to be doing that. My platelets are back to normal. My white counts were like that on a chart and now they've leveled off. They're not perfect, but they've leveled off.

**Larry D. Cripe, MD:** Great. You would be what we call the best case scenario.

**Q3:** And I'm 78.

**Jean Ridgeway:** I think they're recording the session, so if people are speaking if they could speak into a microphone.

**Larry D. Cripe, MD:** Okay. Good. Alright.

I saw another hand. No? Yes, ma'am. Speak in your microphone.

**Q4:** Okay. Yeah. My husband was on… he started in January with MDS and actually the eye doctor found hemorrhaging behind his eye and then when he had the blood count checked, his hemoglobin was six. They did test. He had the chromosome or something so they could use the pill. He was on the Revlimid 10 milligrams for 21 days and then the whites went down. We waited. Then he went onto five for about 20 days and then he went for the 2 ½ and then he ended up with squamous cell carcinoma. So now, he has to go through radiation before they can start chemo in the vein. Now, is this chemo in the vein going to do pretty much…? It was a rare side effect of the Revlimid and apparently he got it. So, is the chemo in the vein going to be doing that stuff to him, too, or is that kind of a little bit different side effects from them pill?

**Larry D. Cripe, MD:** I would not equate the chemotherapy he's receiving with what's happened with the pill.

**Q4:** Okay. We were told that.

**Larry D. Cripe, MD:** No, I'm sorry. What he's likely to experience with the chemotherapy and what he experienced with Revlimid, I would not… those are not going to overlap very much. So, I think the… I think it's very legitimate to ask the question because Revlimid works in several different ways, but one of the ways it seems to work is change the interaction between cells and many of those cells are immune cells. So, you could speculate that many the Lenalidomide

predisposed him to develop the cancer, but it probably did not cause the cancer in my opinion. So, you sort of have… the way I would think about this is parallel paths. He now has a cancer that needs treatment and that cancer should be treated in the best of all possible ways and it may or may not interrupt the treatment of the MDS. So, you could… I could imagine both scenarios. I could imagine where maybe they would just say, well, let's stop the Revlimid, get the squamous cell carcinoma treated, use transfusions or whatever to get him through that and then once you're at the other end of that then you could turn your head… your attention back to the MDS.

**Q4:** Now, that's what I think… He starts the radiation Monday and they want to hurry up and get that done and get the skin cancer in check and then he will be starting the chemo because he's been getting transfusions like every couple weeks? A couple units and that and plus with this he's been getting and we were told this part of the MDS, the aching and stuff of the joints. Now, I don't know if that will change then after the chemo starts.

**Larry D. Cripe, MD:** Yeah. I think it's… So, there are definitely what we call case series that suggest people with MDS have more rheumatic symptoms on average. I always encouraged people and my physician colleagues to not jump too soon to the idea that MDS is responsible for symptoms like that because most people get through without symptoms like that. So, I think it's always about saying okay, it could be the MDS, but I will occasionally think about other causes that should be considered just to make sure you don't miss another cause of whatever the joint pains or the other symptoms that sometimes people with MDS have and almost certainly I'd just would say that receiving chemotherapy for another cancer when you have MDS just makes it a little more difficult in terms of the blood count recovery and the effect on the bone marrow.

**Q4:** Yeah. They said they will do the radiation and then after that's all done that they can't do both together then they will start the chemo, but they're in a big hurry to get that radiation done because of his blood transfusions and that.

**Larry D. Cripe, MD:** Sure. That makes perfect sense to me.

**Q5:** Okay. Well and there's probably how many spots of this squamous…

**Q4:** At least 20 some...

**Q5:** All on his head, his chest and his ears. You know what I mean? Well, there's a lot.

**Larry D. Cripe, MD:** So, it's a skin squamous.

**Q4:** Yes. Squamous cell carcinoma. So, they looked at doing surgical removal, but he's having some problems with bleeding. So instead of that, they're going to treat him with a radiation. They removed one from his chest and then after that the bleeding was somewhat uncontrollable. So, they're going to do the radiation for the rest, the remaining spots all over his face and head.

**Larry D. Cripe, MD:** It sounds like you folks are in for some challenges to get through all of this. I just, once again as I said earlier, I think it's always good to help your doctor be as useful as possible by making sure that whatever options you're thinking about that there's a clear sense of the goal of that option and what other options might exist, but yeah, good luck. I wish you well.

**Q6:** Quick question. My husband here that's on Vidaza was at 19.5 blasts when he was diagnosed. Doctor hoping to treat him from MDS, but he said it was about AML at the time and this all occurred about three months after he had a pretty good physical with no show. Can it onset that fast and become AML that fast?

**Larry D. Cripe, MD:** So, I encourage people not to use terms like 'fast.' I don't think looking at the timing. So to me, the analogy I try to use is it's the princess and the pea phenomenon. So, almost certainly the disease did not go from not being there to being there in such a short period of time, but if you think about the readout is a complete blood count. So, the complete blood count… So, the disease could be there and is slowly the blast percentage is increasing at some rate, but until it effects the blood count readout, you wouldn't know that and it's sort of like a tipping point. So most people who are otherwise healthy will do pretty well with a hemoglobin nine, eight or even lower and… but that hemoglobin didn't become low over night. It took a while but… and people adapt to it, but finally someone will say well I am short of breath or I am bruising too much and will get checked. So, I wouldn't think that the biology of it was that fast as much as just the period of time when it could be connected. So, one of the things that… when I first started training almost everybody we treated with acute myeloid leukemia had a very high white count and that's the where the word 'leukemia' came from. Now, the average person with acute myeloid leukemia or MDs really has modestly low blood counts because the blood count is so commonly obtained when people see doctors, but I don't think there's any… I wouldn't infer any information from that three month period of time.

**Q6:** Thank you.

**Larry D. Cripe, MD:** I think you were… Okay.

**Q7:** In my case, I'd go see the family doctor every six months. He'd look at the CBC, eh, your hemoglobin's down. This went on for a couple of years. Says finally… He says, "Go see this hematologist." He ran some tests and he says, "You may just have a normal low blood count." Says, "Don't come back unless you're sent." Three years went by and they kept going lower and lower. He sent me back and bingo they had to do a bone marrow, but they literally filled the table with blood test tubes. I started counting and got to nine and missed some, but those showed nothing. It wasn't until they did the bone marrow. It was just long and slow. Mine is deletion 5Q.

**Larry D. Cripe, MD:** Yeah. That's very common. It's just we don't know why. We don't know how and I would say your story perfectly illustrates it really doesn't matter. So if they had done

the bone marrow tests years before when your hemoglobin was here, they would have just said well, you have it. Let's just watch and wait until it matters to you.

**Q7:** A good friend of mine lives out in rural Indiana. He, I guess, felt fine till one day he had an argument with a chainsaw. He kept all his body parts, but when they did the routine blood test they said, "You're in a heap of trouble." His platelets were at 120, going down 50 a month. So, his accident helped him really. It's the hard way, but apparently he had no problem before that.

**Larry D. Cripe, MD:** Right. Very common story and I forget who said that, but many people walk in and that's one of the things we work through with people is they say, "I know I'm sick, but I don't feel that way and I hear what you're telling me, but that's not how I'm living my life," and yeah, there's a big disconnect there.

**Q7:** I had no symptom. I began to get tired, but I could cure that. Sit down and take a nap, but…

**Larry D. Cripe, MD:** Alright. This side of the room is awful quiet. We're among friends.

**Q8:** We asked about bone marrow transplants for him and we were told he was too old and he's 68. Is that the way you feel?

**Larry D. Cripe, MD:** No.

**Q8:** Well, 69 now.

**Larry D. Cripe, MD:** I feel that the discussion about bone marrow transplant should be had with almost everybody and that… So, I'm a big believer in just laying out all the options from soup to nuts and then letting people help us make the decision. So, my transplant colleagues are fearless in terms of who they will offer transplants to and so I think it's worthwhile to have a discussion with… if you haven't, with a transplant physician to understand his or her perspective. Now, I believe that most people as the age 70 approaches when they hear about a transplant are less interested in pursuing that, but I'm a big believer in early on at least offering people a chance to have that conversation because it just seems to me it's a different conversation to say, "No, you're too whatever, old, infirm," as opposed to saying, "Well, let's look at it and then let's get back together and talk about that information." So, I don't… Now, let me say this in all honesty. If I were taking care of somebody… When I take care of somebody who's above age 65, I will mention transplant. I will mention that as a rule. I do not recommend transplant, but that I think it would be worthwhile for you to say… you to meet one of my colleagues who does transplants just to hear about it, but so… yeah. I don't know. Does that make sense?

**Q8:** Yes. He had noticed transplants was mainly for people in their 40s and 50s and so that he was too…

**Larry D. Cripe, MD:** Once again, I'm looking at my colleague. That's very true depending on what type of transplant you are talking about. So no, I would encourage you to just ask to meet with somebody and have that discussion. I think you'll feel better about it. I think… So the other thing I would say in case anyone in the room is sort of stuck there is that the other thing that transplant used to be is sort of like we have exhausted everything else, so let's do a transplant now. That is not, in my opinion, and I'm not a transplant doctor. So, I don't really have a dog in this fight. That is not the way to approach this. The way to approach this is to say would I receive a transplant? And some people for them it's unequivocally no, I would not and then you can just push it off the table, but I'll tell you even for those people who push it say, "No, I don't want to," I will every third or four visit just say to them, "Has anything changed? Do you want to talk about that again?" but please try to avoid saying, "Well, I will do a transplant when things get bad enough," and I'm not saying you're saying that because when things get bad enough the risk of transplant have gone way up, the benefits gone way down and then it makes no sense. So, I think for most people with MDS it would be good to have a discussion about that. Yes, sir.

**Q9:** What's the five years survival of transplants?

**Larry D. Cripe, MD:** Well, of course, it depends.

**Q9:** On the average.

**Larry D. Cripe, MD:** Right. Of course, it depends, but you have to be… you have to say what is a five year survival. I'm not going to give you a single number because even when I don't give the people I take care of numbers they make numbers up. I'm not going to give you a number. There's a tipping point. So, somebody with MDS with very risk MDS may on average survival seven to 10 years. For those individuals, I think most of us feel the risk of transplant and the harm from it suggests that they're not going benefit, but so you can't compare their outcomes with the outcomes of people who are less likely to do well, but in general we say to people and most of the ones we do are now these mini transplants. So, they're not the intensive transplant. We say to people the chance of dying in the first nine… six months or so is about 15 to 20 percent. Most of that's carried by complications from the transplant. Some of it's from the disease itself and then if you look at a year, a year or so out it's probably about 30 percent or so. So, it's not… but I want to say is that it's not for me to decide on your behalf. I mean, I think if… maybe you've all had these discussions. I'm always amazed when people push me for numbers and I will give them numbers, a number that I may think looks pretty good will be devastating and a number I think is pretty devastating will be well… They'll say, "Well, at least it's not zero." So, the bottom line is we need to figure out a way to help people with these diseases get the information they want, process the information relative to their values and goals and then make a decision.

**Q9:** The reason and I ask I read the various drugs and it seems like when survival hits 40 percent, the doctors go nuts. This is really good. Of course, considering it probably is, but that's 60 percent nonsurvivable.

**Larry D. Cripe, MD:** You and I are exactly on the same page. I don't think… First of all, I don't think numbers help that much. I think really it's about what's likely to happen if I do it, what's likely to happen if I don't do it, what's the worst case scenario, what's the best case scenario for both of those options? It is not… People all the time will say to me, "Well, if I were your mother, if I were your brother, if I were you," the honest answer is I don't really know the answer to any of those questions because I don't… There are people who… I can just tell you in 25 years of doing this, I never get it right. So, I mean, it's just so… what you do is you keep saying to people, "Well, tell me what you're thinking." So, it's rare that I can say to somebody you absolutely need to do this. This is the best thing for you. I can say, "I think it's the best thing for you. What do you think?" And this goes not just for transplant. This goes for everything we do. I mean, it's not… I know medically what I'm taught is the right thing to do, but you're human beings and, I mean, it may not be right for you. So, I would not get focused on numbers. I would get focused on I have… So, I'm very visual. I think about these as paths. I'm here. I have a goal here. What are the paths and what is it likely to look like on that path?

**Q9:** I just wondered about the survival because I've read the process and it's long and it's difficult and I think there's a time at which if you know there is very little chance of survival why bother that the path is just too hard and no benefit.

**Larry D. Cripe, MD:** With all due deference, I'm going to leave this discussion, but I just would recognize that you have made several very personal statements. So, no benefit is a very relative term because there's never a point at which you can say to somebody there is no benefit. So, what I tend to tell people is based upon my experience… So, I talk about pushing and pulling and opening a door. I try to avoid ever pushing somebody. There are some people who I think I really wish I did not have to do this for you, but they say, "Look. I listened. I want to do this." So, I open the door and I'm like okay, let's do the best and then there are other people who are reluctant, but I sort of think based upon on how I know them and what's likely to happen that they need a little coaxing, but ultimately it's your decision. I mean, that's what it's got to be and so for you to say no benefit, that means I, (Attendee), see there's no benefit and I, (Attendee), don't want to do that.

**Q9:** Perhaps I should have said no or little benefit.

**Larry D. Cripe, MD:** No, no. You can say no benefit, but you need to remember that's you looking at that. Sorry. I don't mean to be so feisty with you.

**Q9:** I'll forgive you.

**Larry D. Cripe, MD:** Poor (Attendee) is sitting there, "Oh, God. This is why we didn't invite him back." (Laughing) But if I could leave you with one message, you really have to help your doctor communicate about these things and it's awkward, but in the end your doctor will appreciate this. I guarantee you. I love it when I walk into rooms. I write everything down for people. I give them lots of things that I'm thinking I love it when I walk in a room and someone says, "Sit down. I have a list of questions," because that means… that gives me an ability to know what you're thinking, so I can really address what you want to talk about because otherwise I do a lot of busywork just so you know you visited a doctor, but it's not really helpful. Yes, ma'am?

**Q10:** Is it possible to have an accurate diagnosis of MDS without a bone marrow biopsy?

**Larry D. Cripe, MD:** Yes, but I would not encourage that. So, you can… So, I can look at the blood film and I will have a pretty good idea of whether it's MDS or not. I will have virtually no acrid idea. So if there aren't blasts in the blood, I will virtually have no accurate idea about how many blasts there are in the blood or in the bone marrow and that's a critical determinate of how I would approach that disease, but it is possible that you can… you could look at the blood. So, somebody with an anemia who had large red cells, you could do a FISH analysis on the peripheral blood. You could discover the Del 5Q and you could well statistically the Del 5Q is favorable, so I doubt that you're going to have high… So, you could do that, but I would not recommend that. I would at least get one bone marrow test to make sure.

I don't think anyone is so jump in so please…

**Q11:** With respect to transfusions, iron overload is trying to control the amount of iron in my diet kind off folly because it's overshadowed or is it worth looking at?

**Larry D. Cripe, MD:** Well, so when I take care… which I don't do as much anymore. When I used to… When I first started my practice taking care of people with hemochromatosis who have… my understanding from them it was miserable trying to control dietary iron that finding foods that are not supplemented with iron. So, that's one… I'm not going to say it's folly, I'm just going to say there are trade winds you're fighting against. Two, a transfusion of iron has 250 milligrams… a transfusion of red cells has 250 milligrams of iron on average. Your dietary intake of iron when you're iron replete is less than a milligram a day, I'm not sure you can really reduce that. So, I think mathematically it's not very… So, this is a controversial opinion and I'm not against… and I don't want to imply that this is right, but I think that we are more interested in the implications of iron in the body because we have drug companies who have developed products to remove iron from the body. I understand that statistically when you look at populations of people that the more transfusions you have there's a decrement in survival. I understand all that, but I rarely use and the few times I do I'm underwhelmed with how much we lower the iron and I'm overwhelmed with how many side effects people have, but once again I

think that's a discussion that you really just say if I use X, I will experience Y and make that decision, but I'm not a big iron chelator person.

**Q11:** Thanks.

**Larry D. Cripe, MD:** Yes, ma'am.

**Q12:** So, the stages of MDS, are there like specific… do they call them stages and how do we understand… It's my dad… our dad and then this is my stepmother and so I live in Tennessee now and they live in South Bend, Indiana. So, I'm kind of a little bit removed, so we send a lot of information. So, I don't know… I didn't know if it was stages, is it levels, how do we determine what…? How do we understand where he's at based on the information?

**Larry D. Cripe, MD:** So, thank you for that question. It is not staged in the sense that we stage people who have cancers from solid organs. Staging for people with cancer with cancers or diseases like lymphoma actually is really the anatomic extent of the disease and it's done that way so the surgeon or radiation oncologist can decide can they cure the disease with a local treatment. So, we don't stage MDS in that way. So, we don't… that does not determine that way because there's never a surgical… it's never localized. So, I was probably not clear. So what we do is we do something called risk stratification and there's… and like I said I tend to at a maximum think about low, intermediate and high risk disease and we think about two risks – one, the risk of dying because of the low blood counts and two, the risk that the disease develops into acute myeloid leukemia. So, people with higher risk disease, one of those two things are more likely to happen on average in the next year to three years depending. Conversely, people with lower risk disease some of whom can live for a decade or longer maybe needing transfusions. So, it's really the risk stratification is more about predicting what's the likelihood of happening. So, what I would do is ask your doctor what is the risk stratification and that's done by the bone marrow blast. It's done by the level… counts in the blood. It's done by the chromosome analysis and that will give you at least a broad category of what's likely to happen.

**Q12:** Yeah. I think that…I think he's in the intermediate.

**Q13:** The blasts were like… I'm trying to think is it five percent or point something. It was not the lowest one, but the next one according to how many blasts he had. He had like three bone marrow biopsies in this year. So, we've got a… gave us a sheet on that.

**Larry D. Cripe, MD:** Yeah. So, I think the most useful one is really would include the blast percentage and the cytogenetics and then the levels of platelets and the hemoglobin level. So, I think I would say that going in for the full… but I'm sure your doctor has that information and can just easily answer it.

**Q13:** She's been really good. I mean, she'll talk with us for a whole hour and give us all the paperwork on everything we discuss. So, she's pretty good.

**Q12:** Yeah. My sister, she lives in town where my parents live and she has gone to several… a couple of meetings with the oncologist and the last meeting they went which was when? Last week? The week before last?

**Q13:** When we found out… Yeah…

**Q12:** It was at 20 percent.

**Larry D. Cripe, MD:** The blasts were at 20 percent?

**Q13:** No, they weren't at 20.

**Q12:** Twenty, it's leukemia. It was like 12 or 14 his blasts were. Twelve or 14 percent.

**Larry D. Cripe, MD:** So, one thing this falls under the rule, I think, of helping the physician to communicate, so and I'm sure you guys have this in your booklets. I would (inaudible 50:29) that time your physician is spending with you, I would just say can we go ahead and plug in numbers into these values so you have them. So, there's agreement and that will… I always caution people looking at the survival curves and stuff is the statistical analysis and you can't be overly reassured or overly pessimistic about it, but it would give you a qualitative sense of what's likely to happen and then you can start, once again, sort of segregating well if the best case happens and the worst case happens then you can start, I think, anticipating those sort of things. Did someone else… Alright.

Well, I feel like we're getting ready to say goodbye to one another. Thank you very much for allowing me to join you this morning and I'm sure you'll enjoy Jean's presentation. So, take care. Best of luck to all of you.

(Applause)

**Jean Ridgeway:** I need a couple of minutes just to get… I do have slides. So, I have to work with the IT guy. That's not something I'm gifted in, so we're going to work on that and feel free to get up and use the restroom or grab another cup of coffee and maybe reconvene. Give me five minutes. Sound good?

(Break 51:59 – 59:49)

**Jean Ridgeway:** Alright. What do you think? Most people here? Alright. How about if people begin to find their way back to where they were sitting or you can sit somewhere else. That

would be fine, but either way how about if we come together and regroup and go forward for the rest of the afternoon? Sound good? Alright. I'll keep talking.

So, my name is Jean Ridgeway and I am the exact opposite of Dr. Cripe. I am totally Type A and I like slides and so we're all a little different and just because it's different doesn't necessarily make it wrong, but we're very different people. We have very different styles and I think some of the beauty of working interdisciplinary with my physician colleagues as we come around the table to have discussions is that there's variability and some people like certain things and some people like others.

So like him, let me give you a little bit of an introduction. Some people, some friends in the room know me a little bit. So, I am a doctorally prepared… No, I finished my doctoral degree last year and so I find myself what's considered an advanced practice nurse or a nurse practitioner up at the University of Chicago. So, I have been practicing in malignant hematology for 30 plus years, believe it or not and I look in the same mirror as him and I say, "How can such a young person be doing this for such a long time?" The University of Chicago is set in Chicago. We're on the south side 35 miles from north to south. I work way on the south side and you know I live way on the north side. So, I drive the Dan Ryan and all those other good things. So, I'm married. You'll see my husband walk in here. He is not a medical person. So, he is with me today. My practice consists of I work as an outpatient provider, work with 10 different physicians. I've worked with a key group for over 25 years all in MDS and acute leukemia and find myself in these past dozen years or so being more absorbed into the stem cell transplant program. So, people had some questions we'll talk lots more about that. One of my key interests really is transplants and acute hematological malignancies for those people age 65 and older. So, I find myself drawn to that group for a variety of reasons, but so be it that's where I am. I also have the unique opportunity in the past few years I'm also what we call the Director of the Advanced Practice Provider. So, I have 30 nurse practitioners and physician assistants who report to me. So, I have four children. I've been trained well. No bad behavior alarms me any longer. So, I'm here today to really talk about Myelodysplastic Syndrome and lots of different aspects of it to answer your questions. Again, it is informal. I have slides. I think it's nice to have some slides. It gives us some talking points. If you haven't picked up one of their books, *The Building Blocks of Hope*, please do so if not for yourself then somebody that you can pass it along to.

So, what I'd really like to do is go around the room and give you each an opportunity to introduce yourself. I'd like to know where you're from. That would be helpful for me. I'm not a geographical genius, so if you tell me where in Indiana, I know South Bend is north of here and a little west, but if you'll help me understand kind of where you are. My husband and I drove here. I had clinic yesterday, finished up at about 5:00, finished some charting and phone calls, I was finishing up some more this morning, but we drove here this morning. It was a lovely drive. We didn't see any deer, knock on wood, they didn't see us which was a good thing and so if you'll introduce yourself let us know whether you are the patient, a family member, a caregiver and if there's one thing that… what really drew you here, it'd be interested… I'd be really interested in

knowing that and let me know if you like dark chocolate or milk chocolate. So, any chocolate is good for me, but I will tell you that I lean towards the dark chocolate. So, why don't we start over here to my left? This is (Attendee). Please tell us you name.

**Q14:** I'm (Attendee). My wife (Attendee) is with me. We're both retired and we're in Cicero, Indiana which is about 32 miles straight north from here and dark chocolate.

**Jean Ridgeway:** And are you the patient?

**Q14:** I'm the patient. I'm sorry. Yes.

**Jean Ridgeway:** You're the patient. Okay.

**Q14:** And I had read about the MDS Foundation on the web and got interested and I'm very glad I came down here today.

**Jean Ridgeway:** Welcome. Caregivers have to introduce themselves, too, and remember one of the things the Foundation does is we do collect the information. Some of these are podcasts. I'll tell you that one of my patients who came to one of these is actually one of our stem cell transplant patients. She got admitted on Wednesday. Her name (Attendee) and she said, "Please make sure that people speak in the microphone so I can listen to the podcast." So, go ahead.

**Q15:** (Attendee) and I'm…

**Jean Ridgeway:** Speak right into that microphone or we really can't hear you. I'm so sorry. Don't be shy.

**Q15:** I'm the diet consultant.

**Jean Ridgeway:** She's the diet consultant for (Attendee). Okay. Raise your hand if you need a diet consult. Welcome. We're skipping a few chairs.

**Q16:** I'm (Attendee) and I'm the patient and we live in Carmel, Indiana and I'm here because my wife said we should come.

**Jean Ridgeway:** Okay. You are a smart guy.

**Q17:** I'm the wife, (Attendee) who said we should come.

**Jean Ridgeway:** And, (Attendee), who's the patient?

**Q17:** My husband's the patient.

**Jean Ridgeway:** Okay. (Attendee)'s the patient. Carmel is also has a very good swimming program. My kids all four of them successfully swam Division 1 programs. I came to this IUP Y pool more times than I care to admit. So, my car was almost on automatic because I headed south on 65. Welcome.

**Q17:** Thank you.

**Q18:** I'm (Attendee). I'm the patient and we're here because we've been to previous conferences and I came back.

**Jean Ridgeway:** And where are you from?

**Q18:** Dayton, Ohio.

**Jean Ridgeway:** Dayton, Ohio. Milk or dark chocolate?

**Q18:** Dark.

**Q19:** I'm (Attendee). I'm his spouse and caregiver, I guess, which isn't much right now, but we'd had been here sooner, but 70 was shut down for an accident totally.

**Jean Ridgeway:** That's frustrating. Welcome. Dayton, Ohio. How far away is that?

**Q19:** Usually, about two hours, but much more today. Dark chocolate.

**Jean Ridgeway:** Dark chocolate for you.

**Q20:** I'm (Attendee). I'm a local representative here with Celgene Corporation and I'm involved in both therapy discussions with physicians that you all see as well as disease state.

**Jean Ridgeway:** One of the things I think all of us on the media get a little bit biased, but really our partners in the pharmaceutical industry are really key in developing further therapies for many different disorders and that they do help to underwrite educational symposiums like this one. So, the pharmaceutical industries are not our enemies. They're our coworkers. You're next.

**Q21:** Well, I was waiting to hear if (Attendee) likes chocolate.

**Jean Ridgeway:** Yeah. Was that… milk chocolate? Okay.

**Q21:** My name is (Attendee) and I like milk chocolate, too, but I represent BMT InfoNet and we are a support organization that provides accurate information and emotional support for people

who before, during and after transplant and I live in Fishers, Indiana, but our organization is actually based in the northern Chicago suburbs and I have a table out there and everything on it is for your taking for free except we do have books on sale today for $10 on transplants, but everything else just take.

**Jean Ridgeway:** Okay and just out of… so people know in this room, how do people become a registered donor if people are interested in becoming donors?

**Q21:** They are best to Be The Match and that's a separate organization, but we work hand in hand with them and they go bethematch.org, I believe and it starts with a cheek swab and then there's several different levels of testing from there. So, Be The Match can really point you in the direction or get you the testing swab and get you in the registry.

**Jean Ridgeway:** If you're not a patient.

**Q21:** Yes and that would be a national registry that also connects with global organizations, too.

**Jean Ridgeway:** So, BMT InfoNet is your organization.

**Q21:** Yes.

**Jean Ridgeway:** Okay. Welcome.

**Q21:** Thank you very much.

**Jean Ridgeway:** Did you say dark?

**Q21:** No, no milk.

**Jean Ridgeway:** Oh, so sorry. Alright.

**Q21:** But you haven't had Mabel's Milk Chocolate from New Jersey, so till you have that…

**Jean Ridgeway:** Alright. There is a place up the road called Donald Sense Candies. That's a local entity that has good chocolates, but anyway I digress. Go ahead. You're next.

**Q22:** My name is (Attendee) and my father is a patient, but he's just not here. I'm from South Bend, Indiana and either chocolate.

**Jean Ridgeway:** Either one.

**Q22:** Either, any, all.

**Jean Ridgeway:** Very good. I know where South Bend is.

**Q22:** They have a South Bend Chocolate (inaudible 1:09:57).

**Q23:** I'm (Attendee) and it's my husband that has the MDS and these are the daughters that brought me up here and milk chocolate.

**Q24:** And my name is (Attendee). I'm originally from South Bend and I currently live in Knoxville, Tennessee and I'm up here to get a little bit more info and then shoot up to South Bend to visit my dad for a few days. I'm very interested in getting some more information and a better understanding of how the MDS functions and what the numbers mean on the blast and the cell count so and I prefer milk chocolate also.

**Jean Ridgeway:** In the corner, ladies.

**Q25:** Hello. My name is (Attendee) and I'm here because my sister is a patient and I want to be as supportive as possible with her illness.

**Jean Ridgeway:** Very good. Where do you live?

**Q25:** I just moved back to Indianapolis after 30 some years of living elsewhere and I love dark chocolate.

**Q26:** I'm (Attendee). I was diagnosed eight years ago and I'm doing really well. I have a mild case I'm happy to say. So far no transfusions, nothing. Just a little chemo pill daily and dark.

**Jean Ridgeway:** Dark chocolate and are you local here in Indianapolis?

**Q26:** Yes.

**Q27:** I'm (Attendee) and we live in Washington, Indiana which is two hours south of here and my husband, (Attendee), is the patient, but so I found this online and I told him we need to go to find out more.

**Jean Ridgeway:** Well, welcome.

**Q27:** That's why we're here and I like milk chocolate.

**Q28:** I'm (Attendee) and I'm the patient and I'm here because she told me I was going to be here.

**Jean Ridgeway:** Another smart guy.

**Q28:** And I like milk chocolate.

**Jean Ridgeway:** Milk chocolate. Okay.

**Q29:** I'm (Attendee) and I'm the patient. Just diagnosed this past summer. So, I'm really in need of a lot of information and hearing all of your experiences has been very helpful even though I know each experience is different, it still helps give some dimension to what is likely to be had and I live in Illinois near St. Louis and it's definitely dark chocolate and lots of it.

**Jean Ridgeway:** So, Southern Illinois. Is that…So, that's like…

**Q29:** No. We're part of the St. Louis metropolitan area.

**Jean Ridgeway:** Okay.

**Q30:** I'm (Attendee), (Attendee)'s my wife. I'm her partner in this disease.

**Jean Ridgeway:** That's true.

**Q30:** We live in Highland, Illinois, not Highland Park although we get mail all the time from Highland Park. Everybody knows about Highland Park. We're only 10,000, but we're right on 70 at the 30 mile marker. So, we just drive out and come straight here and anything Dove.

**Jean Ridgeway:** Anything Dove chocolate. Okay. Welcome.

**Q31:** Okay. My name is (Attendee). I'm from South Bend, Indiana. I'm the patient and just did… give me milk chocolate.

**Jean Ridgeway:** Milk chocolate. Now, (Attendee) has been to these groups before. How many?

**Q31:** Eight.

**Jean Ridgeway:** How long have you lived with your illness?

**Q31:** Right now we're just talk about around 10 years. Around 10 years.

**Q32:** Finally diagnosed nine years ago but it took a year and a half to diagnose it.

**Jean Ridgeway:** So, his wife says he's been diagnosed about eight years, but it took about a year and a half to get the diagnosis. Nine years. But it took about a year or a year and a half to get the diagnosis.

**Q32:** We're thinking at least 10 years it was affecting (inaudible 1:13:56). So, I'm (Attendee). We're both from south Bend and I'm here supporting (Attendee) with his journey on this who knows what's going to happen disease and definitely milk chocolate.

**Jean Ridgeway:** Alright. Well welcome to everyone. I am somebody who likes to live by schedules. That goes along with my Type A personality and on our agenda it says we're going to break at noon which is in 30 minutes for lunch which is true and I would say during that time feel free to get to know one another, chat, ask questions. I don't know I'll have to ask Dee if there's any way that you all can share information if you're interested in swapping E-mails or addresses or phone numbers. I'll ask if that's a formal thing or if we just pass around a sign-up sheet like we did in grammar school. You start at the top with your name. We'll find out. So and then we'll restart again at 1:00.

And we'll talk through these slides. Sometimes what happens is a lot of the questions get answered as we just talk through them, but the majority of the information really is in this book, in *The Building Blocks of Hope* in one way, shape or form. Remember that besides the physical book that you received here if you go on the Internet, you can get a PDF file ie, an electronic file. You can download it to your tablet or your computer so if other people in your family are interested and want more information it's a good place to steer them to is the MDS Foundation's website. So, that's a good thing.

So, this is just to let you know that there's a very large contingent of people who for many years now have been looking at the disease of Myelodysplastic Syndrome and what we do know about MDS is that it's considered heterogenous. That means it's not the same. So, when you talk to other patients and you think about scenarios. Remember that you're not cookie cutter people and neither are your diseases. So, you come prepackaged. We all come with a history, a health history, a life history and that plays into how your disease is able to be controlled and some of the side effects as well, but it's a very unique. It shares many similarities, but it has a whole spectrum of what the disease can behave.

So behind me is really just a list of the International Nurse Leadership Board. Back in the late '90s when then this was all getting going there was a core group of us who felt like as providers who are supposed to help patients we didn't know very much and so we can best help patients if we're well educated. So, the goal of this group is to really help educate nursing colleagues internationally so that when nurses work with physicians and patients that they're delivering a consistent, accurate message. So, lots of people all over the globe work on this and they're a great group and these type of meetings happen internationally. They happen in Greece, in Italy, in Germany and the Netherlands because MDS has no boundaries. It has no gender boundaries,

no economic boundaries, no geographical boundaries and so people across the globe continue to experience what you all are experiencing just in a different place.

So, when we go through this some of the things that are answered are trying to understand the diagnosis of MDS. It really is considered a rare disorder or a rare disease. Most people when they get diagnosed have likely had a difficult pathway to get the diagnosis. People talk about physicians noticing that they have anemia and they just kind of track the anemia for a while. Anemia is common and there are some anemias that can be driven by blood loss. There's some anemias that can be driven by nutrition, B6, B12, folate, iron deficiencies and there comes a point in time where your primary care physician many times then says well, I really don't like the way your anemia is behaving or perhaps you're continuing to be more anemic or neutropenic, the white counts are going down and then they refer you over to that hematologist. So, more than one patient talks about the tightness in their chest that they feel when they arrive at the hematologist oncologist like why is that word up there? I'm going for something related to blood. Nobody talked about cancer to me. So, it's an intimidating environment to walk into and I would say working as a healthcare provider, I work in an environment that's like going to a foreign country without knowing the language. So when I go to Mexico, I can't read the signs. I don't know what the words mean. I have no idea what they're saying. I'll be a little here and there and so it's the same thing as you begin your journey in healthcare. Everything is new and everything is different and you may be an expert in your career, but you're now going to be the novice when you walk into this and not only the novice, but you're feeling very vulnerable because you may feel absolutely fine and someone saying to you, "You have something that is potentially life threateningly wrong with you." So, there's a lot barriers to overcome to kind of get to the root of the information and get to those questions like Dr. Cripe was talking about like was is this, what are my goals, what can I expect.

So, understanding MDS. So, we'll talk about how it's diagnosed, treatment options, I will discuss some different treatment options. Some folks in this room are on pills. I'm going to assume… it's never good to assume, but Revlimid or Lenalidomide is the pill that's approved and out there for treating MDS and some of these other agents, Vidaza and Dacogen. A little bit about new treatments. What's out there? There's a lot out there in clinical trials. In December, the very first week of December, if you're on the Internet what you'll begin to see about the 5th or the 8th are news flashes and newsbreaks because every December the first long weekend starting at the Thursday and going through the Tuesday the international… there's a huge international hematology meeting. So, the American Society of Hematology, or ASH, has this meeting the first weekend in December here in the United States. Fifty thousand people or more go. It's a big meeting and what happens at this meeting is lots of educational sessions geared for healthcare professionals, anything hematology – sickle cell disease, ITP, MDS, AML, everything and so research… when people do research it's… I don't want to say it's secretive, but people are very propriety at times about their information and when they divulge it. So, there will be a lot of studies that information will come out for the first time about new drugs that are under development, breakthrough kind of happenings in hematology. So if you're on the Internet then

put in 'ASH meeting' or 'ASH updates in December' and you can kind of get like the popups from it. So, a lot of things will roll out there, way too much then they do these little video vignettes and all kind of stuff.

So, what's new and then we'll look at consequences of blood transfusions. We talked about a little bit about iron chelation. What about transplant. So, I told you that I do a lot of work in transplant especially for older patients. We happen to run something called… it's called the TOP Clinic, The Optimization and Performance meeting. It's an interdisciplinary meeting. All of our patients who are over the age of 60 who are undergoing a transplant where their cells are going to come from someone other than their own. So if you get your own cells that's called an autologous transplant. That's standard of care for people who have another bone marrow failure disorder called multiple myeloma. We see those people if they're over 70 in the TOPs clinic. We see all of our allo patients the other types of stem cells if you're 60 and above or if you're 50 and above and you're rather ill, in a wheelchair, bedroom, (inaudible 1:22:50) arthritis, whatever and then we meet as a group and we every specialization tries to look at this person. We all have strengths and we all have vulnerabilities and so we try to improve on the strengths and build up the vulnerabilities. So, that's what we do and the patients come in and they meet then with… they meet with myself for a medical evaluation. They meet with our transplant clinical coordinator, Dr. Arts (sp? 1:23:17). They meet with physical therapy and all types of tests are done to really gauge peoples' fitness. They meet with our social worker. They meet with the dietician. They meet with infectious disease. They are given many quality of life indicators and neuro psyche testing so all these different tests. Many times that are done before and then at the end of that four or five hours the patient leaves, but then we all get together for about an hour and give our perspective and see if there are common themes that come up that need to be addressed before someone goes to transplant or perhaps make the decision that maybe the risks for this person are too great and this person shouldn't go to transplant so and at times that does happen because it's an intensive risky treatment that is difficult. It can be easier if you're 40, but when you add a few decades onto that it definitely goes a little bit difficult. Our oldest transplant patients for an allogeneic transplant at my center has been 75. He's doing fine. So, not easy, but he's doing okay.

So, we'll talk about that a little bit and then how can I keep myself healthy. I would say first off the bat it really depends on your hematologist, but you should make sure you get a flu vaccine. You hear me talk about this all the time because people die of influenza and if someone doesn't have a great immune system like those folks with MDS, they need to get immunized and everybody who lives and interfaces with that person. So what you want to do is create a cocoon so wag your finger at your family members and say get a flu shot. Okay? Now, they don't make you sick because they're not made with… they used to have horse serum in them and people would talk about like oh, my gosh. I never get a flu shot. I get so sick. Bah humbug. So, that's… So, it's a dead vaccine. Your arm gets a little sore. Are they perfect? No. The CDC puts together a combination of what was popular last year, but the other thing it does do is if you get a cold, it will decrease the length of days that you have the cold and it will decrease the severity of your

symptoms. That's well documented. So, get a flu shot and make everybody else in your house get a flu shot. Give them my phone number if they start giving you a hard time. So, that's one of the good things.

Alright. So, look through the book. It's a complicated book, but it's got a lot of information. So, it's yours to take home and read on the ride home. The people in Carmel, they'll be home before they get to the third page, but that's okay and so we'll go forward with that.

So to start off for people who are newer to the group, I guess I think it would be interesting for people who have been kind of around in the environment what do you tell your friends when you say, "Oh, I have this MDS?" What do you say to people? Do you share your diagnosis?

**Q33:** It really depends…

**Jean Ridgeway:** It really depends.

**Q33:** Just the environment.

**Jean Ridgeway:** If someone was to ask you what is MDS, what would you say?

**Q33:** Well, I just make it simple and I say it's cancer of the blood.

**Jean Ridgeway:** Cancer of the blood.

**Q33:** Then you don't have to go into the fact of it could be (inaudible 1:26:47) just all the other stuff.

**Jean Ridgeway:** So, it really is a blood cancer. There was a lot of debate over the past number of years of is it a cancer or isn't it a cancer. It is a cancer of the blood and why do we say that? Go ahead, (Attendee).

**Q33:** I was wrapped in the argument of whether it was cancer or (inaudible 1:27:08) back 10 years ago when they started getting into that and I wasn't getting any…

**Jean Ridgeway:** You weren't getting any love were you?

**Q33:** No. The doctors said it is, but the government with my insurance is saying no, it's not. That's not really a cancer. Well, theoretically, no, but the end result it's going to all end up in (inaudible 1:27:32) anyways and like then when…

**Jean Ridgeway:** Can you speak in the microphone so everybody else can hear you because I have pretty good hearing. I don't want to speak for the girls in the back, but I'm just saying it may be a little hard.

**Q33:** Well, ours is their diagnosis was like I couldn't have Aranesp because that was…

**Jean Ridgeway:** Don't you want to be a rock star and put that microphone right up to your mouth?

**Q33:** You think it'd help?

**Jean Ridgeway:** Yeah. You need to do that.

**Q33:** It just caught for around a couple months there and then they across the ruling that says oh yeah it is a cancer then the FDA said it is a cancer.

**Jean Ridgeway:** Yeah and a lot of it we all work in a world where insurance is going to make us or break us so God help the coder that puts in the wrong diagnoses because it's going to be very difficult.

**Q33:** We have heard that they have finally got this diagnosed as a cancer so that people can draw on their cancer insurance if they have it. We don't, but people who have the cancer insurance can now do it with the MDS is what we've heard before.

**Jean Ridgeway:** Wow. That's good to know. I was not aware of that.

**Q34:** About four or five years ago the *Journal of Leukemia* had an article "Is MDS Cancer or Not?" You can probably find it on their website.

**Jean Ridgeway:** Oh, I'm sure I could.

**Q34:** And they conclude it's kind of iffy, but it is.

**Jean Ridgeway:** When you're a purist and honestly the conversation has definitely over the course of the past 10 years moved more graciously in that direction. It used to be almost an opposition to it, but in biology when we talk about what's a malignant cell and what's healthy cell, malignant cells have a few characteristics that are unlike normal cells. One of them is that they have immortality and immortality Dr. Cripe talked about normal cells do their job and they replace each other and so there's this equilibrium, but that's not true in malignant cells that one becomes two and two becomes four and at the end of 30 doublings or you'd say if I gave you a penny on the first of the month and you doubled the amount all the way till the end of the month you'd have $1 million… more. I'm not good with math, but the number is staggering when you

begin to multiply and that's what happens with malignant cells and it can't very much so happen with those blast cells because the blast malignant cells of MDS are immortalized. They aren't dying like they should. They just continue to replicate.

**Q34:** The author of that article said that diagnosing or writing down a definition of cancer is impossible. He quote a Supreme Court judge who was writing an opinion officially on pornography. The Supreme Court judge says I can't define it because...

**Jean Ridgeway:** Pornography?

**Q34:** Yeah. He said, "I cannot write down a definition," but he says, "But I know it when I see it," and he said that a doctor cannot write down the definition of cancer he says, but when he looks through the microscope he knows it.

**Jean Ridgeway:** But I mean they do share characteristics and so immortality and then something called clonality. So, clones are cookie cutters. One cell looks like another and when the hematopathologist look at the blood and the bone marrow specimens under the microscope one cell looks like another cell looks like another and when the hematopathologist review slides, if you've had more than one bone marrow biopsy what they'll do is they'll take your original slides and they compare them to what the current slide is and if you've had many of them they do it for all of them and they note that you can read these pathology reports in the same molecular markers are on them. There can be something called clonal evolution or can the disease change characters and the answer is yes. So, there can be an evolution and in life things really don't usually get better by themselves. They need a little help and so the same with these diseases that as they progress they don't get better and wishing them away is not what happens in reality of how can we get rid of them, but they can go from the blast percentage which is low to a blast percentage which is higher.

When you look at these slides behind me what we're looking at… let's see if I can do this. See this over here and then this over here. Okay. So, what are we looking at? So, this is what the hematopathologist looks at when they look under the microscope. So, this is what we consider low power. So if you wear cheaters or magnifiers there's one set and you can read the print on the paper and then you pull out your bigger… you pull out the bigger handheld magnifier. It's even bigger. So, that's what you're seeing here. This is more low power and this is more high power, but all these cells if you're a hematopathologist you're kind of like a counterfeit expert. So when people study money to know what's a counterfeit and what's an original, what do they study? They study the original then they can identify what the counterfeit is or what's abnormal. So, hematopathologists are trained to know what's abnormal and normal. So, they know the normal and then they know the abnormal and they're able to look at these cells under the microscope and say oh, yeah, that's a mature red cell and yeah, this is a mono blast. This looks like here's… they have two different nuclei in one cell and that's abnormal. So, that's dysplastic

and this over here looks like something else. So, they can really go ahead and identify under the microscope of what it is because that's what they do. That's what they do and they're great at it.

And so what we know about it is that so what is MDS? So, MDS represents a group of bone marrow cancers and, again, the whole spectrum. We'll talk about different labels because we talk a disorder of MDS called 5Q-. We can talk about RAEB2, refractory anemia with excess blasts times two and we'll tease that out a little bit to help you understand, but you should… I would encourage all of you to know your diagnosis, get copies of your pathology report. They belong to you. They're your information and when you have a pathology report, usually how it's written… So, we'll talk about a bone marrow report. It'll give a summary statement at the beginning, at the very beginning and then they give pages of description. So, don't get lost in that unless you want to go to sleep because it's just kind of… it's language for a hematopathologist and the conversation between the hematopathologist and the providers, the physicians and the APNs, we can read that and be able to say this is what it means. Don't get caught up in all the dreary details. There are some details that are important.

So and we also know that MDS is clonal. One line. And we'll look at another slide, but the M in MDS means it's a myeloid disorder. So, the myeloid cells are cells that make our white blood cells, our red blood cells and our platelets. So when we see abnormalities in any of those we know that's where it's coming from. That's from the myeloid. So, that's where the M in myeloid is and then it's just not one disease. It's got a lot of different variations. Nobody in this room has the same disorder if you start thinking about it.

So, what happens? So the cells themselves have an abnormal shape and that's where the dysplastic comes from. So an abnormally shaped cell is like if you put tires on your car that are not round and instead are elliptical or square. Do they work? Yeah, kind of. Do they work great? No. Is the ride kind of bumpy? Yeah. So, dysplastic cells are the same. They're not normal shape and what happens in part of that processes is that they're unable then to carry out the function that they're supposed to. So instead of having nice round tires on your car going down the road, no problem, there's a problem. So as these cells are functioning, the white blood cells even though you might have some are less able to fight off those bacterial infections. It's more complicated but that… but that's true.

Platelets, same thing. People may have 50,000 platelets. Neurosurgeries can be done if you have a platelet count of 50,000 but like your dad had a biopsy or a removal of something even though they have platelets they're dysfunctional. They're not doing their job and people can bleed a lot and you would think wow, that kind of catches people off guard. Even with a relatively safe platelet level people continue to bleed and anemia, people may have an okay hemoglobin, but still just not feel great because their red cells are not able to carry the oxygen that your cells need to function. So, you're tired. Your muscles ache because they're just not getting enough oxygen. It's harder to think. The brain's not getting enough oxygen and so they're dysplastic and as we begin to have lower amounts of cells, we have something called cytopenia. So, that's another…

that's just a language and all it means is low blood counts. So in MDS we talk about three cytopenias. The most common one is anemia and that's a decrease in your red blood cells. If you look on your CBC that's measured by your hemoglobin or your heart depending on your center. We look at hemoglobin, but it's easy to remember because there's always a one to three ratio of hemoglobin to hematocrit. So, if your hemoglobin's 10, your hematocrit should be 30. So if your doctor says your crit today is 18 you know you're really anemic because hemoglobin's going to be about six. So, anemia is the most common cytopenia with Myelodysplastic Syndrome. Eighty-five percent of all MDS patients have anemia. Really common.

What happens when you get anemic? Well, your oxygen ability to provide for your tissues is diminished. So, what needs oxygen? Well, the first thing you should think of is your heart and so your heart is responsible for pumping that blood to everywhere and so people who are anemic many times the fatigue that goes along with is just the global stressor of not having enough oxygen, but tissues work better with oxygen and that's why you want to avoid any damage. If you don't have enough oxygen, I mean, if worse comes to worse then low levels of oxygen in the blood can lead to organ damage and that's at all costs that's what a blood transfusion is trying to avoid.

**Q35:** I have a question about…

**Jean Ridgeway:** Be a rock star.

**Q35:** Very often I'm told what my oxygen saturation is. Am I correct in understanding that that means the red cells that I do have are working when I get 100 percent they're working as hard as they can which doesn't speak to the fact that I don't have as many as I should.

**Jean Ridgeway:** Correct. So, he asked about oxygen saturation. Nowadays when you go into the doctor's office, they usually put a little clip on your finger. They do your blood pressure then they do the clip and then they get nervous because one of the other things that can happen is if you have low oxygen our lungs are responsible for filtering breathable air to get the most oxygen. So then they worry about is there a lung process. So, they'll always check if they get nervous when it gets below like 92 to 90, take some deep breaths, etc., but there's no exact matching that goes with hemoglobin and oxygen saturation because you can have profound anemia. You can have a hemoglobin of seven and still have an O2 sat of 98 percent. That's your body's way of adjusting, but one of the other things it does to adjust is that when you're profoundly anemic, you're tired. Your body is saying we're not going out for a long brisk walk today. We're not taking the storm windows off. I'm not going up and cleaning the gutters out and physically your muscles tell you you can't do this and thinking can be harder as well. So, those are the consequences of having anemia.

So, two other cytopenias with MDS if your white blood cell count is low we call that neutropenia. There are five major types of white cells, but the neutrophil is the most common

and really very important. Their job is to fight bacterial infections. So when you're neutropenic, your doctors often will say make sure you're washing your hands really well, stay away from sick people because your ability to fight infection is lower. The best thing you can do to fight infection besides everybody getting a flu shot at your household is to wash your hands. So when you go anyplace in public and you touch the table and then you rub your eyes like I do you can induce a virus or a bacteria. So, you want to try to keep hands away from face and then just keep those hands well washed. Soap and water's great. Purell or some type of other waterless thing in your pocket is also a good thing. There you go.

Question.

**Q36:** Yeah. I think some people don't realize when you do wash your hands and I'm on my husband for this you wash your hands and you never shut the faucet off with your hand. You take the towel and do it and you don't touch the door. I worked at St. Paul's for 16 years. So, yeah.

**Jean Ridgeway:** The same thing when you leave a public bathroom. If you're using paper, keep the paper, open the door and then dispose of it. Little tricks. Anyway. I think people are much more aware of good handwashing and better hygiene. We see the store wipe the Clorox on the cart before you walk. So, those are always good things.

And then the last one is thrombocytopenia and that means you have low platelets and consequences of low platelets are easy bruising, easy bleeding. So if you have something biopsied even a bone marrow biopsy, you know, they're going to have to put a pressure dressing on that, have you lay on your back for a bit because when we puncture your bone to do a bone marrow we use a pretty large needle and I can't really stick my finger back in there to plug the dyke. So, that's how we do it. We hold pressure. We'll go ahead and do bone marrow biopsies if your platelets are 10,000. We may go ahead and ask for a transfusion. The recommended time to give somebody a platelet transfusion is 10,000 or lower or if they have active bleeding. Other things to think about is many people develop heart disease as we age and so or if they have stints in their heart they have to be on a medicine called Plavix. So, Plavix is a platelet inhibitor and you need to be aware of if your platelets drop below 50,000 usually the Plavix has to be held. There are a number of new agents that for people who also develop blood clots because even if you have low platelets you can develop a blood clot. It's very interesting, but all those things have to be closely monitored. So, drugs like Coumadin, Arixtra, Lovenox is an injection. Those have to be carefully monitored when you've got low platelets, even if you don't have low platelets. So, those are the three cytopenias.

So in MDS, you can have a cytopenia that affects only one line which would be… it can be the platelets, it can be the white count, it can be the platelets. It could be two or it could be all three. So if you have more than one, they say you're pancytopenic. That's just another way of saying everything is down beneath the normal levels. That's what pancytopenia means.

Okay. On the money. Why don't we take this opportunity to break for lunch and then we'll reconvene… Are we eating in here? Okay. We'll eat in here and then should we say do you want to restart at like 12:45? In 45 minutes. If it looks like we need more time than that that's fine, but lunch is outside.

**Dee Murray:** It's outside and you can bring it in here.

**Jean Ridgeway:** And you can bring it in here.

**Dee Murray:** Anyone, if you could just fill out these evaluations that I just gave you and just give them back to me. Thank you.

(Lunch break)

**Jean Ridgeway:** … talk about what is MDS and some of the characteristics and it is now 1:45… 12:45 and we'll finish up at 2:00. I think it's fair. That's what time we said we'd be done, but if you want to stick around afterwards and ask some additional questions, I'm fine with that. My husband, a/k/a my driver, he's okay with it, too.

So in talking about what is MDS, again, remember we talked that it's a bone marrow failure disorder and in general as the disease progresses the bone marrow failure… the bone marrow itself the functionality of it begins to decline. So, what does that mean? It means that you can see worsening of blood counts, increasing needs for transfusions, perhaps increasing amounts of infection. Something that's really telling us in more than one way of just the CBC that things are declining.

So, this is, I think, a really cute cartoon. I like this and so all of our blood cells began at hemopoietic blood cells. So, hemopoiesis is the big word that means blood formation and this is just a little character, a cartoon that says in the beginning there was the stem cell. So, let's talk a little bit about how like blood is formed and just to tickle your ear a bit about like stem cells. In the media sometimes we hear things about stem cell research. So, stem cells are the most immature cells period, but there are different types of stem cells and what we hear about in the media oftentimes is embryonic stem cells and that's when the egg and the sperm come together for the first seven days as those cells are together and they're very all immature. They're all stem cells and they have yet to become dedicated to becoming one type of cell lineage or another and so what we hear about a lot is this embryonic stem cell research because what they're trying to accomplish is can they create the environment to make all cells nerve cells so that we can have a cure for spinal cord injuries. Can we make all cells liver cells so that we can create a cure for liver cancer? So, that's embryonic stem cell research and I will tell you that it has not been successful, but stem cells from blood or hemopoietic stem cells and what we know about them have been very successful and so when we look at a potential therapy for some types of MDS

and for some candidates, some patients or a different leukemias we look at stem cell transplant because what we're giving to the patient is stem cells. Sometimes it's known as bone marrow. So, I heard before we all joined together someone was saying like what's the difference between a bone marrow transplant and a stem cell transplant. So, when the whole field of transplant began the only way that we could gather high quantities, big quantities and densities of stem cells were to remove them from the bone marrow micro environment. So, we all have stem cells and they're found mostly inside of the bones. The easiest place to get it from is our pelvis. That's why we do the bone marrow exam in the pelvis and so actually as people got a bone marrow harvest they didn't used to use a drug called Neupogen. They would take the donor to the operating room and put them to sleep and a provider would work on either side doing about 100 bone marrow aspirations as they went up and down the posterior iliac crest to gain enough sample to be able to successfully give that to the… make the donation. Is that done anymore? Yes, in rare cases. Ninety-eight percent of all stem cell donors now collect. We collect stem cells from donors via their blood and how we do that is the person whose donating is given a growth factor called Neupogen. Some of you may have gotten that just to boost your white blood cells. It's a growth factor and it increases the production of white blood cells and the most immature cell is the stem cell. They get high doses of it. It's an injection given once daily and it looks like an insulin injection. So, it's very small and then on day five they go to the collection center. If the donor is over in Europe that's fine or if it's local and if you've ever heard about a… so any of you have received a platelet donation, those platelets were given and when someone gives a dedicated platelet transfusions, they go to a blood donor center and an IV is started in one arm and a return IV is put in the other. So, the blood is taken out, whole blood, and it's centrifuged and depending on the product that they're collecting be it platelet or stem cells by weight it's collected into a bag and it looks like a blood transfusion and the rest of the blood products returned into the arm. A little more sophisticated, but that's really what it is and people sit there for about six hours and many times a one day collection is all that's needed for them to donate stem cells.

So in this picture, here's the hematopoietic stem cell and what we know about it is that there are two major families of cell types in the bone marrow. There's the myeloid cell and that's the one we've been talking about and we know that myeloid cells then become… these are the grown up cells out in the peripheral blood. These are all white blood cells, neutrophils, basophils, eosinophils. These are platelets. That's the platelet precursor. It's called the megakaryocyte and then red blood cells. So if you follow the lineage of when a stem cell becomes… and this is then along the line of maturation. It's a myeloid progenitor cell and then many influences force this creation. Now, on the other family is something called the lymphoid cell. So, this is a lymphoid progenitor cell and then grown up cells in the peripheral blood and the lymphoid family are lymphocytes T and B cells and if you have some friends and family who have a bone marrow disease called multiple myeloma that's a B cell malignancy because B cells secrete immunoglobulins and they do that via a plasma cell. So, that's where that disease comes in. So what happens in MDS then is with… so we start getting an accumulation of immature cells. So, what does that mean? That means instead of following this line and growing up into a normal healthy cell, the cell gets arrested or stopped in maturation. So, one of the first cells as they begin

to grow up is a blast cell. So, blasts are big cells and it's normal to have some because that's a normal process of cell maturation. So if you have up to five percent blasts in your bone marrow when a bone marrow exam is done it's considered normal, but if you cross the threshold of more than five then that's abnormal. So, when bone marrow reports are read the pathologist will make a comment on how many blasts you have and so know that in a normal cell it's up to five percent. So, what happens in Myelodysplastic Syndrome is that we begin to have an accumulation of immature cells and what happens is that as they begin to grow they continue to proliferate like the penny that gets doubled by the end of the month. So, you're going to have a lot of cells in the bone marrow and they begin to crowd out all of the normal cells and they begin to crowd out the normal hematopoietic cells as well, so we can also see subsequent decrease in production.

And then what do we see? Well, the downstream consequence of that is that we begin to see cytopenias. All the things we talked about – lowering of hemoglobin, the platelet and then the white cells.

So, what about the diagnosis? So, (Attendee) said it took the medical community a year and a half to get his diagnosis. I heard someone else over here talking about that they had anemia that their doctor watched for a while, watched for a while and then it came to a point where you saw a hematologist and then you got the diagnosis which is not uncommon. Oftentimes one of the biggest frustrations that patients and families have with the diagnosis of MDS is that they feel it took a long time and questions about should something have been done sooner. We talked about that earlier. Would it have been beneficial or not oftentimes are the questions.

So once you do see the hematologist, a couple of things get done. They draw lots of blood. We love to draw blood in hematology. A little doesn't go a long way. We want a lot of it. So, we draw the CBC, but then we draw other things because red blood cells need nutrients to grow and so some of the things we check are levels of fixable anemias. We check iron. We check folate. We check your thyroid because if you have a little bit of a low thyroid it can have anemia. We check testosterone because that also can play into it, but then the question earlier was do you absolutely have to have a bone marrow biopsy to be diagnosed? If you have a great hematologist, no, but the party line says yes. You got to have at least one and so studies that are done from the bone marrow a lot and that's because what we see in the bone marrow is not what we see in the peripheral blood. So, there's this huge discordance. It's like looking at your house from the outside and opening it up and walking around on the inside. It's really very different. It's all the same, but it's very different and so what do we test? We look at the number of blasts and the hematopathologists look at these things under the microscope and they're able to tell us how many do you have, what do you have. They look at something called cellularity. Cellularity tells us how much tissue is producing cells and it's always 100 percent minus your age. So if you're 60, your cellularity should be 40 percent. If you're 60 and you have a bone marrow and your cellularity is 100 percent of 90 percent that's too much. So just like children are hyperactive, you have a hyperactive bone marrow. So, we say you have a hypercellular bone marrow which

means lots of activity and you say well, then why don't I have great blood counts? Because somewhere along the line there's either sequestration or that's kept in the bone marrow or there's some destruction going on. So, you can have really a lot of activity and a lot of cytopenias or you can have something called hypocellular and that means you just don't have a lot of tissue. So, you're just not making a lot. So, that can happen, too.

Other things that get done. We check something called cytogenic. So, we all carry DNA and sometimes if you're watching TV, you hear about people asking who's the baby's daddy and they do this cheek swab and why do they do that? Because we all carry something called constitutional DNA. So, we can do mine and then we can do somebody else's. It's very, very different and that's constitutional DNA, but what we're looking for in the bone marrow is not like who's the baby's daddy. We know that, but what we want to know are there abnormalities within the abnormal cells that help us understand the signature or the characteristics of the disease. So some people in this room I've heard say they have a 5Q-. So, what's that? Chromosomes, 46 we have, 23 pairs. The last pair of chromosomes identify us as a male or a female. So the XX people in this room are like me, we're women. XYs, those are men. So, that's your 23rd pair. So, they number them from one until 23 and actually if you were to look at a picture of all of your DNA starting with the number one they're the biggest and all the way down to the end they get smaller and they kind of have… they have a funny shape to them, have a unique shape to them where they have only arms. So, no legs on cytogenetics and they P arms on the top and they have Q arms on the bottom and in the middle they have skinny little waists. It's called a centromere and so if you have a 5Q- what that's saying is that on the fifth chromosome, on the Q arm, you're missing a piece. Sometimes you could be missing the whole leg. So, imagine that I'm a chromosome and you're going to cut out a middle slice of my thigh. So if you have 5Q 3.1 to 3.3 which is the 5Q- deletion, there'd be a big chunk of my leg missing. Just… but what would happen is that the rest would refuse together, but it wouldn't be normal and what Lenalidomide for 5Q- does is it repairs that and disallows that from happening. Sometimes people have whole chromosomes missing like it'll say -7. That means you don't have a seventh chromosome and so if you imagine that your DNA is the mapping telling your bone marrow what the cell's to do if you eliminate one of 23 critical pieces there's going to be a problem and we can further characterize what some of those problems can be. Sometimes you have an extra chromosome. Some people have something called Trisomy 8. That means instead of two chromosomes of eight, you have three. That's what a trisomy means. You can have hyperdiploid. That means you can have instead of 46 chromosomes, you could have 92. So, there are all different types of chromosome abnormalities. If you're bored and you can't sleep you go to Google images and you put in cytogenetics and you put in MDS and you can see a lifetime's worth, but there are people that's what they do. So, that's what cytogenetic is and it's important.

We look for iron stain it's the best place to look for iron. How much do you really have and then they do something called a reticulin stain. That helps the pathologist understand a little bit more about characteristics and then all of that gets put together and there are two major classification systems. So, we didn't talk about… this isn't "staged." It's classified and all diseases have their

own little language. MDS is no different. So, the first classification system was called the FAB and that stands for French, American and British and those are the hematopathologists who for a long time were all looking at the same thing, but they didn't have a common language to speak and so they all got together in the early '70s and they said we got to like… we're all seeing something that's very unique and we know it's reproducible, so they came together and they identified something called the FAB Classification System and there were five major subtypes at that point in time of MDS. Four of the five revolved around anemia. So, you had RA which is refractory anemia; RARS, refractory anemia with ring sideroblasts. They're beautiful little cells. That's another great Google image. Then there's RAEB, refractory anemia excess blasts. So, you know it's more than five percent and in the world of FAB, people used to call acute leukemia if you had 30 percent blasts in the bone marrow. That's been revised. Now, they say 20, but the difference between RAEB1 and 2 was how many blasts. More blasts up to 30 percent was RAEB2 and then there was RAEBT and that's in transformation, transformation to acute leukemia. So for some people MDS can evolve to acute leukemia. About one in four they say. What's the difference? It's the number of blasts. Depending on where you are in that trajectory is what happens. Can they be treated similarly? Yes with hypomethylators. And the last one was called CMMoL chronic meylomonocytic leukemia and so that was the fifth subtype. Now as science evolved, more and more became known about MDS and more and more sophisticated tests moved from the academic environments out to the community and so cytogenetics is now done everywhere. It used to just be done at the academic centers. Now, there's labs all over the place and so they began to say wow, there's like cytogenetics became more common back in the late '90s and then into the 2000s and so the World Health Organization so more hematopathologists got together and they developed this secondary classification system that built on the FAB called the WHO. So, that was last revised in 2008 and it's under revision right now and what's happening is we're seeing a further expansion and a further description of the fine lines of what's your diagnosis. So, Dr. Cripe talked about like people who were kind of into the minutia of details and then he said he was a clumper. He was a low risk or a high risk. So, there's a coupe ways you can look at it. I think it's important to know your diagnosis and then to understand where does it fit in the risk stratifications, but usually in that pathology report they'll give you a diagnosis. They'll say pathology consistent with refractory anemia with excess blast type 1. One other important distinction with the WHO criteria is they said that acute myeloid leukemia or AML, they now define it at 20 percent not 30 percent. So, that was a little bit different.

So, this is more of that. So, you can see that here's the FAB way over here and then the WHO and then 2008 there's more, blah, blah, blah, don't even bother to read the typing and then the dysplasia where does it occur and then the number of blasts. So, there's a lot out there. Leave it to your doctor kind of learn the speakeasy of what it means. There's good descriptions in the *Building Blocks* so that you can go back and further identify it.

So, most of the time when people find out they have some type of disorder the really question of what does it mean to me ie, how is it going to impact my life. Is it going to shorten my life? Do I

have to have any treatment? Is there anything to be done is the next valid question. So, some very smart people who had been working in MDS for a long time said we need to really understand what is the disease of MDS and how does it behave. So, I'll tell you that 25 years ago people paid this much attention to the disease of MDS. They thought, eh, it's very rare, there's no treatments, we're not going to talk about it and so the people who in the '80s and '90s were studying the disorder from their hematopathology colleagues were looked down up very much so and so but some of the pioneers and one of them being Dr. Peter Greenberg who worked out of Stanford for many years has been involved in this effort and so the IPSS scoring system if you've heard about like what's my IPSS score that's where this information comes from and so what he and some of his colleagues did was they looked at all the patients from like the '80s and '90s, but now remember the first approved treatment didn't happen until 2004. So, only 11 years ago. So, these were all untreated people with MDS and they tried to understand the characteristics of the disorder. So, they looked at all these patients, almost 900 patients and they said these are the things that really help the clinician predict how the patient's disease is going to behave. Now, everybody's crystal ball is a little bit cloudy, but theirs was pretty clear at this time and so what they discovered was the three major pieces that help understand the disorder were the number of blasts in the bone marrow, the number of cytopenias, so red, white and platelets, and then the number… what is your cytogenetics and then they came up with something called a Risk and Prognosis and that is really used even today for how do you select a treatment.

So, I had a handy dandy app on my phone because I do this on a daily basis and it's really you can plug your numbers in. Now, it's free to download. If you just go to app store and you put IPSS you can just download it in. So, the IPSS score when we have a new patient come to us we look at all that information and because in order to go forward with the discussion that's what you need to do and this is also in the Building Blocks and it's on the Foundation's website. So, not to worry, but we can plug those numbers in and then we come out with a score and people… There are two scales. There's the IPSS and then there was the IPSS-R which was a revised score and it further expanded out the risk categories.

So, things that you might already know. What's the average of MDS? It's in the early 70s. Do we see people with earlier onset? Yeah, we do. We see people in their 30s. It remains an incurable malignancy and allogeneic transplant that means cells from someone else is the only potential cure. So, I work in transplant. I'll tell you it's a very difficult therapy. The complications can be difficult, but people survive. We just finished our celebration afternoon with our transplant patients about a month ago. We had over 200 people there. We have people in their 70s who have survived many years with their MDS and AML transplants as well as myeloma. So, people do survive. It's the right fit. It's the right therapy for the right person and I think I'm amiss at not saying to you that if you get a response from a physician that you're unsatisfied with you go for a second opinion. The MDS Foundation can help steer you to a Center of Excellence where people at those centers see MDS patients. So, sometimes people come to these and they're newly diagnosed and their doctor says something like, "Oh, wow. You're like my second MDS patient. I don't have anybody else with your disease," and that

doesn't exactly instill confidence in you. It's like if you're going for open heart surgery, do you want the guy who does two a year or do you want the guy that does like two a day. You want the guy, the expert, and that's fine and we live in a culture that allows us to do that. So, I would strongly encourage you to seek another opinion and talk to the people here if you're looking for somebody good they can probably point you in the right direction.

Another question that sometimes people ask is when people reach the end of the trajectory of the disorder, how do people die? What do people die of with MDS? So, I'd say to you that since… to put the puzzle pieces together one of the things to think about is the average life expectancy in the United States for men, I believe, is 63. For women, it's… not 63, it's 73, but for women it's like 80. So, nobody gets out of here alive. We are all finite beings and considering your mortality is something that we all need to do, but this is a disorder that oftentimes can happen to folks later in their life and some people are more healthy with this disorder than others. Some people have a lot of illnesses. You can think about people in your own life that have diabetes, they're big smokers, they're already wearing oxygen, maybe they've had an amputation, they've had a bypass, they've had a heart transplant. We have a couple of people in the hospital right now who are undergoing leukemia therapy who have LVADs. Do you know what an LVAD is? Dick Chaney had one. I don't know if he still has it. He got a heart transplant, but it's the mechanical device that circulates the blood when your heart doesn't work anymore. Left ventricular. So, but there are a lot of things can happen and so it can be subsequent to the cytopenias of the disorder. People can get infections or they can if they're done receiving transfusions people pass relatively peacefully. It's not a painful demise or it can just be from something else. If you have a bad heart and your anemia goes down to six, I doubt if you're going to pass the self-induced cardiac stress test and you may have an MI. You may have a heart attack. That could very well happen. So, many times it's the other issues that are going on in life not necessarily the disease, but if you put those two layers together it may be heavy enough that folks may not survive.

And how do you treat people? So, it's watch and wait at first, sure, for some, but depending on where you are on the spectrum, it's going to determine whether or not you get treated because it's very individual.

So, what's the trigger? So, the trigger can be symptoms from anemia. I can't walk across the room. Most people with anemia do okay walking this way, but when you add in going up the stairs or going down the stairs then folks can get into trouble. It's much more stressful on our cardiovascular system to go up and down by lifting the big muscles in our legs.

And as people begin to receive transfusions, how many people in here have had a transfusion? Anybody had a transfusion? (Attendee) got some, (Attendee) got some, the other (Attendee) got some. When you initially get transfusions many times people say, "Wow, I feel a lot better, but now the transfusions don't seem to be working." They don't feel the same boost. Part of that is just your body kind of like getting used to it. Will it continue to raise your hemoglobin? Yeah, it will, but you just don't have that same feeling.

So, when to begin to treat. How many transfusions are you getting and is it time to think about therapy to see if we can change the disease of that. So, that's a trigger.

And then we talked about blasts. So, that sometimes as peoples' counts are… At my institution, we love to do bone marrows. I'm very sorry to say that, but we do them judiciously. If people are on a clinical trial sometimes you have to do them more often just because that's part of the measurement of the clinical trial, but if people are getting standard care then we may give people four to six cycles of Azacitidine and then we may repeat it and, again if you cross the threshold. If you start looking like you're evolving towards leukemia you're needing more transfusions then sometimes that will be a suggestion of when to start.

**Q37:** Who most conducts clinical trials? Pharmaceutical companies?

**Jean Ridgeway:** So, who most conducts clinical trials? It's a blend. It's a blend and what's available at any given institution depends on that institution. So, they're controlled very tightly by the Food and Drug Administration and sometimes physician scientists may be working for a pharmaceutical company and may develop a schema that has gone we say from the bench to the bedside. They've done the petri dish work, they've done the animal models and it's moving towards can we treat people with this? So sometimes pharmaceutical companies will approach institutions and say we have this study and it's using the standard of care plus drug X. We will supply drug X. So the only way you're going to get this new one is if you do it, but it's quite a bit of work for the institutions to hold these things and a lot of paperwork and a lot of people involved and it has to be approved on multiple levels. There's something called an IRB or an Investigational Review Board that individual institutions have as well as pharmaceutical companies. So, they're tightly regulated. They're a very large cooperative groups because anybody in here like a mathematician or a statistician anything like that? So, if you want to see does drug X make a difference? First of all, you have to define what you're looking for and then you got to get enough people on the study that are similar. So, let's just say everybody has refractory anemia and they need transfusions. We'll make that our clinical trial and we're going to say we're going to treat them with drug A or B. We want to see if there's a difference. So, the statistical people will say in order to be able to say it makes a difference, how do you really show that? What are the numbers? You may have to enroll 800 patients. So even at IU, it would take them a lifetime to get 800 people here with MDS with refractory anemia who need transfusions and so they open it up to these large cooperative groups so there's… and that's how those… that's how you accrue that many people. So, they're done everywhere. Some of them are international. Many times they could be international or they can just be within the United States and it takes a long time to get 800 people who fit that stringent set of criterias to see and most of the times bigger places like IU, University of Chicago, Indiana, wherever they have the offering but you got to fit the box in order to do that. So if you're looking at a drug we've got to do these studies with pharmaceutical companies because somebody's got to make that drug and it's got to be regulated. Does that answer your question? Okay.

Anybody in here on a clinical trial? Anybody on a clinical trial in this room? No. Okay. There are a lot of options out there.

So and then you look at some… so you have to look at these other things, too. Performance status. What's performance status? Performance status is how active are you, not how fit you are like you don't have to be doing a marathon, but there's a grading criteria to understand. So when we ask… I'll say to people, well, tell me about a typical day. How active are you? Some people will be like I get up, I have coffee, I read the paper, I walk the dog and then I lay down and I get up for supper and then there's another group of people who say yeah, I don't get up really early, but you know, I walk with the girls, I go to my aerobics class and I volunteer at the library, I do all the shopping and then I make dinner and I fall into bed at nine o'clock. So, how much time do you spend in bed besides just sleeping? So, are you out of bed more than 50 percent of the time? Are you in bed more than 50 percent of the time? So, there's two scales. One of them is called ECOG, the Eastern Cooperative Group and the other one's called Karnofsky. If you're 100 percent on the Karnofsky scale, good to go. You're just like zoom, working fulltime, doing everything. If you're in bed 50 percent or more of the time and you need help getting dressed and with your activity you're at 50 below. ECOG, if you're a zero you're perfect believe it or not. If you're a three, you're spending more than 50 percent time in your bed. So sometimes for clinical trials we have to be relatively fit. You can't be in a nursing home and participate in a clinical trial. That's just… it's not going to work or even for treatment.

Then we have to look at the comorbids. What are those? Do you have heart disease? Are you a diabetic? You look at all those kind of things and then the risk category and then do you have primary or secondary MDS? So some group of people have secondary MDS. Anybody in here have secondary MDS or therapy related? So some folks who get treatment, say, women for breast cancer can develop MDS subsequent to their treatment for their primary malignancy. Men getting prostate cancer oftentimes they get prostate irradiation and the area that gets irradiated is the pelvis. As adults, the majority of our blood cells are created in our pelvic bone and so men who have gotten pelvic irradiation sometimes can develop a therapy related MDS or AML. The timeline is about anywhere from three to seven years afterwards. Breast cancer, they can develop a therapy related MDS or AML. Timeline anywhere from a year to seven years. Hodgkin's disease, that's a younger person's disorder. Folks who get Hodgkin's disease usually in their 20s, now in their 50s and 60s are developing MDS and many times the risk factor can be just that exposure to lots of chemotherapy when they were younger. So, that's a therapy related or a secondary. It's very similar, but it can be a little bit more difficult to treat the therapy related.

So, what are the current treatment options? And so in the United States we talk about something called supportive care. What's supportive care? That's transfusions if you need it. That's growth factors, Epogen. Anybody in this room on Darbepoetin or Procrit? Nobody on growth factors for their red blood cells? What a nice bunch you are. Well, that's another therapy and antibiotics if you need it. Some folks with their MDS have chronic neutropenia. That means they don't have a

lot of white blood cells and you sometimes people think oh, I should be on antibiotic all the time. Well, that's not really true because then we just go ahead and we create further superbugs. So, bugs that and bacteria that are not responsive. So, it's appropriate to get treatment for infections when you need it, but you don't need to be on chronic antibiotic treatment because things get resistant.

So, we talked about a drug called Revlimid or Lenalidomide. So, Lenalidomide is a pill and you take it once a day and so that's one of the therapies. It changes like Dr. Cripe was saying. It changes the way the cells communicate one to another. What about some of the injectable or he alluded to something called hypomethylators. What on goodness sakes is that? So, in chemistry they have methyl, methylene gas and methyl groups. So when I was in high school, we did learn this stuff about chemistry and then when you look at compounds and even with DNA we know that there are various biological structures to all of this. I mean, it's a biological event and so they found that within certain areas of the genes, usually the area of the gene that it's called the promoter region and that's like the brains behind the operation. There can be too many methyl groups. So, just like anything else if you have too much of a good thing it usually can lead to abnormalities and so they found that these medications remove some of those methyl groups from those areas and help restore normal hematopoiesis by changing the constitution and the characteristics of the DNA. That's kind of fancy shmancy but hypo means getting rid of and methyl group. So, there's two drugs that are approved in the United States that are categorized as hypomethylators. One is Vidaza or Azacitidine. You can get that medicine as a shot or you can get it as an infusion. It has the same properties. It all depends. Some people who are getting transfusions and they have a port they don't want a shot. Some people are like give me the shot and let me get out the door because it takes me longer to get the infusing than it does to get the injection. Question?

**Q38:** My question is when we're trying to change the methylation of the DNA, it strikes me that it's got to be a shotgun rather than a rifle. There are specific sites in the DNA that where methyl attaches.

**Jean Ridgeway:** True.

**Q38:** And these drugs sound like they just…

**Jean Ridgeway:** Well, so interesting… his question is are we really kind of casting a broad net and not really being very specific. It's more specific than the traditional chemotherapy and studies actually looking at methylation, Steve Gore on the East Coast does a lot of methylation studies. You still maintain methylation. You don't eliminate it completely. So, the mechanism of action of these drugs is proposed, but not fully understood. So, they are hypomethylators, but they're not global in nature, but that's one of the proposed mechanisms of how they work. They don't understand 100 percent. So, there's Vidaza and then there's Dacogen. So, I heard somebody else in this room saying they started on Decitabine or Dacogen. Similar, not identical.

So, and actually there was… and there continues to be number of providers and there have been a number of papers that show that especially for older patients if you have an AML, if you've evolved to AML and you have a background of dysplasia that Decitabine or Dacogen can be very effective in treating the leukemia especially when you compare traditional therapies for AML in older adults because it's a very difficult disease to treat and the side effects are hard. People get hospitalized. You get really cytopenic and so the Decitabine oftentimes allows people to stay at home. You go back and forth to the clinic to get treatment and how long do they use it? They use it as long as somebody continues to benefit. Now, the trick becomes when you start on these treatments so when to pull the trigger becomes really important because for some disorders they work better than others. He talked about the TET2 mutation which is just another one of those things we measure. Those folks tend to have a good response, but do they work forever? The answer is no and some diseases in some types of MDS they work better. CMMoL, I have a gentleman who's received 60 cycles of Vidaza. So, he's five years on it and his counts are fine. He has not had a transfusion since five years ago. It continues to work for him and he's okay coming in. Now, he only gets it five days a week. The studies did seven in a row and there's lots of different ways to do that. Some people just say I'm only doing five. There's no weekend availability. Give people chemo or it may be come in Monday, Tuesday the subsequent and then that five plus two with the break still gives you seven. So, lots of ways to do it. So, that's one of the ways to do it. So, those are… so we generally will treat someone for at least four if not six cycles before we do the bone marrow to see is there any difference. Are you benefiting or aren't you. Sometimes people will say, "Oh, I feel better," or, "My blood counts are better," but we'll look at a couple slides and you'll see that oftentimes peoples' blood counts get worse before they get better with these treatments. So, we'll look at that.

Other chemotherapy agents. There's some medicines that have been around since the '60s. Cytarabine is one of them. Another word for Cytarabine is Ara-C. In Europe I will tell you that Ara-C is used very, very commonly to treat MDS. It's available. People can do the injections even at home or with a home care nurse. So, Cytarabine in Europe is very much a standard of care. They do things a little differently than us, but and they also have nationalized health insurance and so if the government says this is what you will get unless you can reach into your pocket with a wad of money that is what you get. So, that's part of nationalized health insurance. Clofarabine and Etoposide are other ones. Transplant and then investigational agents speak to clinical trials.

So how do some of the things work? This is a slide we put together a couple years ago. Some of the things on here are available and some of them are still in trial. So, what everything is you spoke of before, (Attendee), is like what we're trying to do is get more specific in treatments. Are there really targeted therapies that we can… and so the MOEA means Mechanism of Action and so these are all targets in the cell that we hope are going to prove effective for people who have MDS. So, here's a drug down here. It was called Ontak and it said that it inhibits miotic progression and induces apoptosis. So what's that? That means as the cell divides, it's stopping that and increasing apoptosis is programmed cell death. We said these cells don't die and that's

what it's trying to do and it was a phase two study and they had an overall response rate of 50 percent. So, half of the people responded, half the people didn't respond and what were some of the side effects? They could have gastrointestinal, they could be tired, they could have nose bleeds or no hematological toxicity. So, that's how you read this slide. Panobinostat is something called a histone deacetylase inhibitor or an HDAC. So DNA wraps around itself like if you uncoiled a DNA strand, it's like 20 meters long. So, how does that 20 meter piece of information fit inside the nucleus of a teeny weeny cell? It winds itself tight like a coiled spring. So if you uncoil that spring in your pen, it's going to be a lot longer than how it fits in that cylinder and histones allow the DNA to wrap. So, histone deacetylase inhibitors allow those to unwrap a bit and then get destroyed. So, those are much more targeted therapies. So, pretty sophisticated biological entities continue to evolve in the world of MDS.

But let's talk about so a little bit more about principles of the therapy in MDS. So an allogeneic transplant is still the only potential cure, but since the average age of many patients who get MDS is 70, many times it's not recommended as a therapy and so I told you that we do an older adult clinic and so we like to help sort out the real issues from just the label of age because age should really never be a barrier in and of itself honestly unless you're 100. Although we started treating an MDS patient, he's 91 this week in clinic. He's pretty spry. He drives himself to clinic. He's a snappy guy. So, it really shouldn't but there is an upper age limit because… you have to have good organ function to be able to tolerate the side effects from transplant because they can be difficult.

The other issue is with transplant is you got to have a donor. So, where do I get donor from? So if you have brothers and sisters they ask you to get your brothers and sisters typed. Why do they do that? Because I get half of my genetic information from my mother and I got half of my genetic information from my father and so did all of my siblings unless there was something that I really don't know about but that I'll just leave it at that and if I have children they get half of their genetic material from me and they get half of their genetic material from my husband. So, there is a chance that the way that things line up, they call it gene shuffling that I have a one in four chance of having the same HLA typing as my siblings. So, there's a one in four chance. Some people are really lucky. They have one sib and they match and some people have 10 sibs and they don't match. Don't know. Now if you don't have a sibling then what we do is people who join Be The Match and they do the swabs, that information gets banked. It's just a computer program and they take what the patient is like and they ask for the International Bone Marrow Registry are there any potential donors. So, they find a donor for me. So then what? So then they contact them. So, (Attendee)'s my donor. He doesn't know this and then the Be the Match calls and says, "(Attendee), we have a potential situation where you could be the match for someone. Would you come in for confirmatory typing?" Then it's a blood test and they match more pieces on the sixth chromosome. If you are a match then what? Then people say yes, I'm available to donate or oh, my gosh, my baby's due next week. I can't donate. So then they got to go to another donor or so it's an ongoing process. We tell our patients that from the time we do a donor search if we identify a patient it's probably a good three to four months before we can get

the cells in hand because I don't know maybe they're out on a cruise. You just don't know. I mean, you're at the whim of the donor. It's a voluntary thing and so everything takes time. Meanwhile, the patient probably still needs treatment. So, you have the patient doing their treatment and then you have this sideshow behind the scenes going on of locating the donor and organizing everything, getting insurance approval and all that. So, it's a process. It's a process.

Age we talked about and all of our treatments require time to work and we talked about this also that blood counts get worse before they get better which is true, but really taking an active part in managing peoples' side effects is the key to get the best response. So, one of the things I would encourage you all to do is as you get into a relationship with your provider, know how to contact them. So, if it happens on a weekend and you're really not… maybe you're a wait and watch kind of person, but something happens. You get a pneumonia and you end up hospitalized. You really need to let your hematologist know. The people in the hospital get really nervous when people come in with low blood counts and they want to do a kabillion tests that may or may not be necessary, but let your provider know and know how to contact them. People, that's their job. They're your employee in reality. So, know how to contact them and know when to contact them. So, what do I tell patients? So, I say to people here's when I want to hear from you. If you develop a fever 100.4 or greater, we need to hear from you. Why? Because of neutropenia and infection. If you really are just not feeling well or developing new symptoms, maybe having lots of bloody noses if you notice blood in your stool, give us a call. We'll see you. If you start having bruising and bleeding, give us a call. We want to see you but if you only remember one thing only remember that if you get a fever see the doctor because that can save your life. The other thing is make sure you have a thermometer in your house. So, that's important.

So, why does it take a while for MDS therapies to work? So, this little cartoon is a gateway into looking at the bone marrow itself. So, inside the bone marrow what you're looking at is a lot of different types of cells. These red little discs, those are good red cells. That's what a red cell really does look like and then we've got some neutrophils but then blast cells and then some dendritic cells as well, but as these cells multiply they begin again to crowd out the abnormal cells.

So, my husband will testify to this that I really think I like to garden and I'm a good gardener but when summer goes on and I get busy, it kind of goes by the wayside. So anybody who's ever had a garden knows that you have to tend to your garden because untended the weeds grow way better than the plants. So, and it's really true about your bone marrow because as the malignant cells are in there they tend to have a survival advantage just like those dog gone weeds and it's nothing I did, but it just happens and with the survival advantage is they will grow stronger, they'll take more of the nutrients and so that the good cells begin to get squeezed out and they just diminish in their vitality. So, that's what's happening inside the bone marrow. So, it's squeezing them out. Then what happens is as you start treatment, you're going to start weeding out those things. So, you're going to get the soil is getting better and you're going to start removing some of those weeds in the garden. So when I've done an aggressive weeding in my

garden then what happens is that my cells that are really good they look kind of spindly. I have to be very protective of them. They will revive, but the magic is time. That's what it's going to take. They'll come back, but it'll take time and so they look a lot worse before they get better and that's what happens to your cells. So during that time that's when you have more transfusion needs or you may be at a higher risk for an infection and it's not uncommon for many people when they begin to get treated to end up in the hospital within a couple of weeks because they get an infection that perhaps might have been lingering for a bit and then when you lower the blood counts then they succumb to the infection. So, there's a lot of frustration because it's like oh, my gosh, did I do the right thing? Did we wait too long and how can I keep doing this if I feel so bad. So, it's a time where you need to remember that it will get better. You just need to get better and go forward. So, starting to clear it out and then we'll talk about that little graph up there, too.

And so this is more of the cells just repopulating and getting better. So, what's going on over here? So, this is somebody's ANC or their Absolute Neutrophil Count. If you haven't heard that term you'll hear it. The neutrophils, again, 80 percent of our white blood cells. So, this person here starts out with a neutrophil count, a good one, 3.2, that's good and then this is treatment. How many weeks are they into treatment? So, most people will get treated for a week and then they won't get treated again until the fifth week. So, it'll be one week on and three weeks off. So, you see the person's ANC really starting to drift and they kind of come up a little bit, but they get way better here at about 12 weeks. So four times three is 12. So, three months into this the person is now bottomed out their counts and started to recover and just kept more of a normal steady state neutrophil count. So, that's what that's about and the bottom slide just continues to say that as your cells get… as your bone marrow gets healthier you get repopulated now with cells that are healthy versus these blast cells that really aren't so healthy. So, you see more red blood cells, more platelets and just the normal neutrophils as opposed to the blast count. So, that's a picture of what's happening.

And this is just… here's where those we say early toxicities. That's a fancy word to say side effects. Some people get mouth sores. Some people get constipation but this is where it can really be hard before you get to here, but know that the hope is that you're going to continue to get treatment and then you'll feel better and the counts will get better. Make sense?

Alright. So, key principles really are that what's the best thing? Time is really… it's the test of time of what's going to show to be better. They get worse before they get better and then what happens in here? How do you get through this? He talked this morning about like having the conversation with your doctor and keeping the communication lines open. Work with them to say like I'm too tired to get treatment this week. I feel like I need another week off. That's perfectly fine or by the way my grandson's wedding is Friday. I don't want to get treatment this week because I want to go and have a good time. I'll see you on Monday and you go ahead and do that and that's perfectly fine. Five days is not going to make a difference in the grand scheme of things. So and making sure that you're getting supportive care both as far as blood counts, yes,

but if you're the patient having MDS you may have some real changes in lifestyle. You may have been a really active person, playing golf and being that person who gets up at six o'clock in the morning and drops into bed at ten o'clock at night and the number one thing that we often hear from people is fatigue and how the fatigue has changed what folks can do with their disease. Would you say that's true? For some people it really is… it's the biggest barrier to overcome to learn how to modify that and so I would say do what you want and make the best of your day. Some people are morning people. I'm a morning person. You're active and doing what you want to do then if you kind of like peter at the end of the day or need a rest then take a rest. If you need to get a lawn service or you have to have your kids come and help and do whatever because you really can't do it then that's what you need to do and to be able to take care of yourself.

Alright. I'm going to show you some slides. So, Sandy Curtain is one of my colleagues. She practices in Arizona. So, she gets the sun and the lizards and the prickly pears. That's what I tell her. We don't have prickly pears up north.

So, this is one of her patients who had four cycles of Azacitidine and so what we're looking at here is here's time on the bottom and this is different measurements. So, the purple boxes are the hemoglobin and the yellow triangles are the platelets and then the purple, this deeper purple is the white blood cell count. So, here's the person way back in June of 2010 and they're coming in here to get a referral. So, what do you see? You see white blood cell count dropping, you see platelet count dropping, you see kind of an up and down of this white blood cell count. So, here they start treatment and what do you see with their platelets? Their platelets really just trend down, down and but then in cycle three you see a lot of recovery because this is the time when you've gotten rid of a lot of the malignant cells. Transfusions were here. Worse before they get better, but then they end up improving quite a bit. Now, this person ended up to go on for a transplant. That's what HCT hemopoietic stem cell transplant. That's what that means. So, they ended up… here they were diagnosed in June of 2010. They ended up about six to seven months later they get a transplant and this is just to say that with someone else's new blood system what happens. Things can really get better. So now, the white blood cell count is six and seven range, the platelets are way up here in the 100,000 and the hemoglobin is way up here in the 13 range. So, here we have someone getting diagnosed, starting treatment. They get a transplant and then they adopt a new blood system. So, it can look a lot different. Make sense?

Alright. Here's one more of her patients. This is a person who's been on Lenalidomide for over 10 years. So, Sandy Curtain used to work with a physician. His name was Alan List and Alan List was one of the key physician investigators when Revlimid was being tested for MDS. So, Sandy got to work with him and so she saw and people would come. They had studies that remember we talked about fitting the boxes for clinical trials? So, they had two different studies – one for 5Q- patients. So, if a patient had 5Q- and they were going to get the drug they'd drive to Arizona and they'd get the drug and they were being followed there. So, they had a lot of patients they accrued to the study. People came for the study and get the medication. So, here's one of her patients for 10 years and so you can see so here's 2002 and, again, the white blood

cell… I'm probably totally in the way, kind of dips down here and here are the platelets. This person's platelets started relatively high and then they kind of dropped down and over time has developed a new norm. Every once in a while you'll see a spike either up or down even in your own blood counts. Your platelets might be 180 one time but usually run at 100. That can happen, but here's the hemoglobin. So, this person has a relatively steady state hemoglobin of at least 12 grams per deciliters but it took a while. This is a year and the person's hemoglobin slowly got better. Is it (Attendee)? Have you been…? Someone's been on Lenalidomide or she left already, but she's been on it for like eight years and so this just shows to you that how long do you take it? You take it as long as it works and does it continue to work it continues to work. So, just some information that people can utilize to stay… to have hope.

Alright. So, what do I say… what do I do to stay healthy? Get exercise. So, I will write a prescription for people to say walk 10 minutes a day. So, try to be as active as you can. Outlooks a lot different for everybody. So, you want to stay active and you want to eat a balanced diet. So one of the things nobody really talked about today is are there dietary restrictions? I wondered if anybody would have a hard time with all the fresh fruit out there, but they didn't. People have really gotten much more liberalized about diet. Years ago it used to be that if you were neutropenic people would say, oh, no fresh fruit and vegetables, but that's not true. If you wash the fruits and you eat a balanced diet you're okay. The only thing of caution is just to make sure that food sources are reputable and even an occasional sushi is okay, but just be careful with the raw fish. The only caveat.

So, avoid infection. We talked about that. Avoid bleeding. We all kind of avoid bleeding at all costs except when you go to the dentist. So if you're going to the dentist and you have a point list dysfunction or you're on Plavix or something you got to tell your dentist otherwise they go at you and your mouth is sore anyway, but if you're going to have easy bleeding you need to make sure that you're letting them know so that things can be adjusted for that. Same thing with infection. Make sure you do get enough rest. I mean, we do need rest but balance your rest and activity. Get outside, go for a walk and make sure you do get your rest. There are a lot of resources over these past 10 to 15 years that are now available to us and so I honestly the *Building Blocks* is really a great place to go. You take it home and you look through it and kind of it becomes your own and, again, you can get it online as well, but many questions that we haven't gone over today are well covered and it's all data based. It's not just what he says or she says, but it's all based by scientific literature. So, it's a great resource and be a participant. If you think that a forum like this is good for you then come back if for nothing else to meet other people and help them do that. These are some links that you can kind of look at online.

**Audrey Hassan:** Included in your packet (inaudible 2:50:26) included in your *Building Blocks of Hope*. (Inaudible 2:50:30)

**Jean Ridgeway:** And then really becoming a partner in your care. Like was mentioned this morning have that ongoing conversation. I encourage all my patients bring… either you bring

index cards to your appointment or you bring some type of folder or you can go to the dollar store and spend a dollar for a spiral notebook, but things make sense when you sit there and you talk to the doctor, but doggone it when you walk right out the door you can't remember what they said. So, write it down and ask them and you can say, "Oh, would you spell that for me," or, "Could you write that down for me?" I write down things all the time for people because what's very common for me I can spell Myelodysplastic Syndrome, but most people can't. So, you want to make sure that you're getting your own information.

So again, it's available for you. It's global. It comes in different languages, doesn't it?

**Audrey Hassan:** Yes. Even Chinese.

**Jean Ridgeway:** Even Chinese and then here's just some other things that you can gather from it from online. I wish I had it kind of like active, but I don't. And these are just other… okay. So if you look at your book, I'm just going to grab this one… Well, I won't grab it, but there's a couple of different settings and tabs on it. The first one is really Understanding MDS and then Looking for Treatment and then Quick Tips kind of answer the questions about what should I do about my diet, what about like constipation or diarrhea or skin rashes. So just hopefully some really helpful daily tidbits and then iron overload talks about it and then the tab number five is really your treatment plan what's going on and go ahead and put your dates in there. You can put in November 2015 blood count stable, no transfusions, whatever. Here's a copy of your CBC. Keep track of it. You can just go ahead and keep it in there and then there's a tab in here that talks about the Foundation and some of the different things that they offer besides coming together as a group. If you haven't gone online and kind of… you can go into podcasts and audio casts. There's teaching tools on there for you to learn and the nice thing about is it's a very reputable website. So, it's not like going to Sally's Story of MDS. You got to be a little careful about that to get information.

So, questions I can answer for you? Too much information? Go ahead.

**Q39:** So the blasts, are the blasts specific to MDS only?

**Jean Ridgeway:** And leukemias.

**Q39:** Okay. So, just those types.

**Jean Ridgeway:** And there's different types of blasts. So with myeloid malignancies they're called myeloblasts. People can have lymphoid disorders like acute lymphoblastic leukemia then they're lymph blasts. So, it is the normal trajectory of an early immature cell to go to a mature cell, but if they get arrested in early development then if you have more than five percent then you start looking in myeloid disorders as disease state. Some people can have less than five, some people can have more than 20 percent. So, that's one of the pieces that we look at when we

consider like what's going on with the person's disease and it's only measured in the bone marrow.

**Q39:** Only in the bone marrow.

**Jean Ridgeway:** Well, you can have peripheral blasts in the blood like on a CBC you may see a one percent, but that just measures the blood. It really doesn't tell you how many are in the bone marrow itself and that's what you have to be concerned about.

**Q39:** So, what is the connection with other like myelo disorders?

**Jean Ridgeway:** What's the connection?

**Q39:** Yeah. Is there any connection between let's say in the same family with the myelofibrosis and then the MDS?

**Jean Ridgeway:** Yeah. So, there's a couple things. So, if you think of three circles. So, there's a circle here. We'll say that's Myelodysplastic Syndrome and then kind of an overlapping circle are myeloproliferative disorders and polycythemia vera and myelofibrosis are part of this more of a proliferative disorder and in the true sense you can have overlapping syndromes or you can have fibrosis in the marrow with MDS. So, you can have one or the others. Remember we talked about what do the hematopathologists look at in the bone marrow? One of the things they check for is something called reticulin. So, reticulin measures how much fibrosis people have in their bone marrows. Usually, it's none. If people have fibrosis it's more of a characteristic of their disease. So, you can have somebody… the most you can have or the most that's graded is 3+. So, it can be MDS with fibrosis because myelofibrosis is a real different disorder. It has a whole another subset of characteristics that people have hot flashes, weight loss, big spleen.

Other questions? Time to… Go ahead.

**Q40:** Does the IPSS score change (inaudible 2:56:52)

**Jean Ridgeway:** So, the IPSS score in its purest form is used at diagnosis. So, they want to understand what's your risk category when you initially present. So, it's not recommended that it's done again to recapture information. It's best predictive of what your disease is when it gets diagnosed.

**Q41:** At every examination they always check his spleen. Is the spleen…? I guess the spleen becoming not normal the result of the drug they're giving your or the disease?

**Jean Ridgeway:** So… is it (Attendee)?

**Q41:** Yes.

**Jean Ridgeway:** So, (Attendee) talked about that they always check his spleen. So, a normal physical exam is that you can't feel a spleen. It's a little organ that sits up on the left side like underneath our lung up here and to have splenomegaly is abnormal. They're with the CMMoL, chronic meylomonocytic leukemia, often times the spleen enlarges. Sometimes the spleen or the liver or both can become extramedullary hematopoiesis sites, ie. they can start to function and create blood cells and with some MDS' people can have splenomegaly as a part of it. It's unusual. It is unusual, but if it's part of the person's presentation then what you're going to do all the time is to feel if it's still palpable. If we have patients that truly have measurable spleens, we measure them because you can measure the spleen tip and it can go from dipping into the pelvis to not measurable. I've had patients who come in with a spleen that's kind of like a baby in there, crosses over the midline and it's a big bulging organ which is abnormal.

Other questions? Let's see. Dee wants an evaluation from you and unless you collect name tags, turn in your name tag and they'll recycle them and use them for the next group. Well, thanks for your attention and have safe travels back. Enjoy Thanksgiving.