

Speakers:

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Susan Hogan: Okay. Good morning. We're going to get started here today. I wanted to thank you all for coming to our MDS Foundation Patient Forum here in Cleveland. My name is Susan Hogan. I'm Operating Director of the Foundation and we also have Tracy Iraca here today. We have a full agenda in store and I'd like to thank Dr. Sekeres and our nurse, Jean Ridgeway, who's in the back there for taking the time to present to you today and answer any questions that you may have. I'll be in the area in case you have any questions about the foundation, so will Tracey. A couple quick housekeeping notes. Those little boxes with the green lights are actually microphones. So when we do Q&A, you could press the little on and off box and we just ask don't put any papers near them because we are being audio recorded and that's what we would get on the audio record and I would also like to thank our sponsors, Novartis and Celgene for making this day possible. Lastly, I think you have some evaluation forms. If you get a chance in the day, we'd appreciate it if you could fill them out and just hand them to Tracey and I at the end of the day. So, I think that's about it. Rest rooms, some of you may know, right out the corridor right across the hall, the first hallway across from the meeting room and I think that's about it. So, I'll turn the program over Dr. Sekeres. Welcome, again.

Dr. Mikkael Sekeres: Thank you. Hi, everyone. Morning. Those of you who know me, I know some of you know I'm extraordinarily casual. So, I'm going to encourage you to stop me if I'm not making any sense. Feel free to interrupt me even mid-sentence. It's really, really, really hard to offend me. People have tried. It just doesn't work. It's impossible to offend me. I'm going to start off... we're going to talk about (inaudible 1:56) just sort of talking about standard stuff in Myelodysplastic Syndrome and make sure we're all on the same page in understanding it and I like to do this actually is what's commonly called the chalk talk. Though we don't use chalk anymore. We use one of the boards and I'm going to ask questions and it's perfectly okay to not know the answer, to say the wrong answer, but I want to try to engage everyone, get us all involved in talking about MDS and make sure we all are thinking about it the same way. I'm actually going to use this and I'll back it up with some slides and then we'll transition into talking about some newer therapies for MDS.

I do with the fellows also. They can't stand... they hate when they're on slides. They like to have something they can take home and read on their own and they don't like to actually have me facing them and asking them questions. It drives them nuts, but I think they learn the best doing this.

What's the... I'm going to start with basic stuff. What is Myelodysplastic Syndromes?

Q1: Bone marrow failure disorder.

Dr. Mikkael Sekeres: Bone marrow failure disorder. (Inaudible 3:08) that's a great (inaudible 3:10). Bone marrow failure disorder. That's absolutely right. So, you referred to the bone marrow. What is the bone marrow normally do?

Q2: Produces cells. White, red and blasts.

Dr. Mikkael Sekeres: Good for you. Fantastic. So, you're about to learn why I went to med school and not art school. So, if this is the bone marrow... this is the bone. Inside is the marrow. Which of our bones make the most marrow? Have the most marrow in it? Make the most red cells?

Q3: The hips.

Dr. Mikkael Sekeres: The hips. That's why we do the bone marrow biopsy there. Right. Hips. Spine.

Q4: The sternum.

Dr. Mikkael Sekeres: Sternum because you can do a sternal bone marrow biopsy also not that I would recommend it to anybody because it hurts. Long bones, head. So, those are also the places where if you have too much bone marrow production, the bones hurt. So, sometimes my patients if they get a growth factor that stimulates the growth of bone marrow, they'll say, "Oh, I have the worse back pain," or, "I've got have hip pain," or, "I got a headache," because those are the parts of the bone that are actually making marrow. So, in the bone marrow you have primitive cells called stem cells. Heard of stem cells. We've read about some of the editorials about the (inaudible 4:28) stem cell research and all this. Stem cell just means the cell can become any cell in the body. If you place it in the bone, it's going to become bone marrow cell. If you place it near the heart, it could become a heart cell. These stem cells... I think about it also in terms of kids going to school. So if you're a stem cell, you're in kindergarten. You have to through steps of maturation going through primary and secondary school eventually making it to high school and then going out into the bloodstream to make a living and you make a living as a red blood cell that brings oxygen to the tissues. You make it as a platelet that helps stop bleeding and you make a living as a white blood cell that fights infection. Basic map of the bone marrow. So with Myelodysplastic Syndrome, you said it was a bone marrow failure condition which implies that the bone marrow is failing. Something occurred. A genetic event occurs randomly. The vast majority of people are not born with this. It happens randomly. It's passed down and eventually it causes the growth of an abnormal looking cell. All of these cells in the bone marrow are called myeloid cells. So, myelodysplasia means... dysplasia means bad growing myeloid cells. So, it starts to grow poorly and when that happens it doesn't make this cell and it doesn't make this cell which means that, for example in this case, your white blood cell count may be low or it might not make this cell in which case your red blood cells won't grow normally and you'll be anemic.

There's a paradox going on here though because why is it happening with Myelodysplastic Syndrome is you make a whole bunch of these abnormal looking cells in the bone marrow and they fill up the bone marrow. So you wind up having too many cells in the bone marrow but too few cells in the bloodstream, but the too many cells that are in the bone marrow are those dysplastic cells. They're the bad growing cells that don't make the mature white cells, red cells and platelets that you need. Any questions about this? This is a basic process of MDS.

So, what's the average age of diagnosis of MDS?

Q5: Sixty.

Dr. Mikkael Sekeres: Sixty. Who said sixty? Sixty. Okay. Is she too high, too low or right on?

Q6: I would say that's the average onset of it.

Dr. Mikkael Sekeres: Average onset at age 60? Too low.

Q6: It's most commonly after 60.

Dr. Mikkael Sekeres: (Attendee) says it's too low. What do you think it is?

Q7: I think it's probably closer to 70.

Dr. Mikkael Sekeres: Closer to 70. So, 70 – 71 is actually the average age. This is a disorder of older adults. Why do you think that is? Why do you think it takes until age 70 to get MDS? Any idea?

Q8: I don't think it takes to age 70 to get MDS. I just think that finally when it manifests itself, enough where your doctor says, "Hey, you have MDS."

Dr. Mikkael Sekeres: That's a great point. So, one thing that's happening is that it takes... So, it's awhile to become clinically manifest is what you're saying. So, you actually first abnormal cell may start when you're 60. So, you may be right, but then it takes 10 years until it grows enough and compromises the bone marrow until the doctor says, "Hey, you're anemic. We better get that worked up." So, that partly what's going on. There's also something else that's going on that's absolutely fascinating. There were a couple of articles that were published in the *New England Journal* in December that looked at a bunch of folks that had schizophrenia. Now, why were they looking at schizophrenia? Well, you can imagine there was a very, very, very wealthy guy whose child has schizophrenia. So, he decided to (inaudible 8:56) hundreds of millions of dollars to research to try and figure out what the genetic cost of schizophrenia was. So, they looked at 17,000 samples from people with schizophrenia and guess what they found about the genetic cost of schizophrenia? They couldn't figure it out. So, all that money spent towards

schizophrenia research really resulted in very little, but there is a guy... this was all given by (inaudible 9:22) Institute in MIT and there was a guy there who said, "You got all those samples. Can I see what you found genetically in all those samples from people with schizophrenia?" and what he found were a bunch of genetic abnormalities being more commonly associated with Myelodysplastic Syndrome. So what you said before about it starting much earlier, it turned if you look at a normal population of patients... normal schizophrenia they don't have bone marrow disorders, but a population of people without any bone marrow disorders you're going to find a certain percentage of those folks have these abnormalities we associate with MDS. Not all of them develop MDS, but if you have that abnormality you're many fold more likely to get MDS than someone who doesn't have the abnormality. So, I may be walking around right now with an abnormality associated with MDS. Does that mean I'm going to get it? No, because it takes multiple steps to get MDS and multiple years.

Q9: Is that a congenital thing from birth that's got abnormality would be present?

Dr. Mikkael Sekeres: It's a very good question. So, congenital means something we're born with. That doesn't imply genetic. So, you can be born with six fingers on one hand. That's a congenital abnormality, but it doesn't mean it's genetic that it's linked to anything that's genetically confined. It means that something just got screwed up in development. So, there are families where MDS runs in the family and we actually were one of the first groups to describe this a few months ago because believe it or not I had a couple of identical twins who came into my practice. Both of them had MDS. So, we tried to figure out what it was about them and we found a common genetic abnormality that was germ lining. They were born with it and they can pass it on as opposed to something that is what we call somatic which means that it just arises spontaneously. Nothing you can do about it. So, we're learning more and more that there are probably more germ line abnormalities that are unique to MDS decades later, but it is not at all common. So, they recently had a major publication on it because it is not at all common. It's a great question.

So, average age is 71. What causes MDS?

Q10: They say smoking can sometimes be a factor as well as there are certain chemicals that also can be a factor or you just get lucky.

Dr. Mikkael Sekeres: Sound like (inaudible 12:02). Average age we said is about 71. What are some of the risk factors? Okay. So, smoking increases the risk. When we talk about risk, we talk about something that's called either the odds ratio or a relative risk. What's your relative risk of getting MDS compared to everyone else in the population who doesn't have that risk factor? So, smoking, the relative risk it is about 1.5 meaning you're about 15 percent more likely to get it than somebody who doesn't smoke. So, going back on an epidemiology also where the geeks who sit around with the HP calculators all the time trying to figure out risks and think about what

causes disease in a population. So, epidemiologists will say it's not a major risk factor until you hit an honest ratio or (inaudible 13:00) of two. So, smoking is a mild risk.

Q10: And they say for secondary if you've had chemo before.

Dr. Mikkael Sekeres: There you go. So, chemo or...

Q10: Radiation.

Dr. Mikkael Sekeres: ... radiation. Radiation therapy that's how we abbreviate radiation therapy. SRT. You read all these articles about how we're doing much better in treating cancer and how people are living longer. Well as they live longer after being exposed to chemotherapy and radiation therapy for other cancers, they had time to develop some of the side effects of that chemotherapy/radiation therapy and one of the side effects is MDS. Chemotherapy and radiation therapy damage stem cells. By definition that's how you kill cancer. Cancer by definition is a fast growing cell. It's a cell that outgrows other cells around it. It happens in a breast, your lung. (inaudible 14:03) cells around it. Happens in the lung, you get a mass that you can see on an x-ray. So, we give therapy that work better in fast growing cells. Well, they work by invading the genetic machinery in those cells (inaudible 14:20). The problem with that they also invade the genetic machinery of other cells in the body that are growing. That's why you lose your hair getting chemo because your hair is always growing. Other cells in your body that are always growing are your bone marrow cells. So, it can cause genetic damage in those bone marrow cells and that years later can lead to MDS. The reason we weren't thinking as much before is first of all we weren't calling it MDS. We were just saying, "Oh, your bone marrow is getting old just like the rest of you." We weren't saying it was MDS (inaudible 14:52) diagnosing it, but the second reason is that now people are living 10 or 20 years after being treated for cancer, they have 10 or 20 years to develop MDS whereas beforehand they only lived three or four years and it was gone. So, chemotherapy and radiation therapy exposure in the past, it accounts for about nine percent of MDS. Lucky.

Q11: Also known as de novo.

Dr. Mikkael Sekeres: De novo is about 90 percent of MDS and then one percent is what we say environmental exposures. Does anyone know what environmental exposures can cause this?

Q12: Pesticides.

Dr. Mikkael Sekeres: Maybe. We don't know for sure. So if you told me that you worked in a pesticide factory and were basically taking a shower in the stuff every year for decades, I would say problem possibly.

Q12: Heavy metals.

Dr. Mikkael Sekeres: If you... (inaudible 15:55) I have lots of patients who constantly say, "You know, it was once in a while I was in high school. I worked on this golf course and they were always spraying the damn thing and I got it on me a couple times." That's probably not quite enough. Heavy metals can cause some types of cancer like liver cancer, but not really MDS that we know of. I'm going to say the epidemiologic studies in MDS are really crappy in the US. So, you may come back from 10 years ago and say, "Remember how you said that thing about heavy metals? Well, you were wrong. It actually does cause MDS." Well, we may figure this out 10 years from now.

Q12: I read an article about a couple that owned a dry cleaning company business and they both came down with MDS, the husband and wife, because of the chemicals they used.

Dr. Mikkael Sekeres: Possibly.

Q12: They thought that there was an association.

Dr. Mikkael Sekeres: What did you say?

Q13: They used perchloroethylene.

Dr. Mikkael Sekeres: So, that's also liver cancer associated with, but it's not the first time I've heard that someone ask whether that's related to MDS and maybe there is something there. Someone else said the one I was looking for.

Q14: Benzene.

Dr. Mikkael Sekeres: Benzene. So, why is it we think about benzene in Cleveland, Ohio?

Q14: I'm not from Cleveland.

Dr. Mikkael Sekeres: Welcome to Cleveland. We're so happy you came.

Q14: (inaudible 17:11).

Dr. Mikkael Sekeres: We're going to learn you something. So, why is it in Cleveland (inaudible 17:16)

Q15: Akron is the rubber development.

Dr. Mikkael Sekeres: So, Goodyear/Goodrich tire, the people who make the blimp. It's a rubber industry and benzene is used in the rubber industry and it was in the late 1960s that a private

practice came and told us in Canton, Ohio right near Akron who was told in med school that in his entire career he would only see one, maybe two instances of what we call Myelodysplastic Syndrome or a rare type of aplastic anemia, had 12 patients in his practice with it. So, he found out they all work at Goodyear/Goodrich tire and it was his testimony in front of OSHA in 1970 that first drew the link between benzene and development of Myelodysplastic Syndromes. So, that sort of stuff is the one percent and, again, I've had a couple of patients where I suspected it was related and this was not... I was a floor manager and a couple days a month I'd be on the floor and see them making the rubber. This was patients of mine who said they were soaking in vats of benzene for years. It was a real major exposure.

Other rarer stuff you may hear about... Do you remember... what was the name of the shoe store that had the... they would x-ray your feet to see whether the shoes would fit. What was it?

Q16: Redline?

Dr. Mikkael Sekeres: No, it's one... I'm from the East Coast and I remember...

Q16: My mom used to take me and put my feet in those things all the time.

Dr. Mikkael Sekeres: What was the name of it?

Q16: I can't remember.

Dr. Mikkael Sekeres: So, going there once or twice and having your feet x-rayed for shoes is not going to do it, but if you're the guy pushing the button on the machine who works there that's going to do it.

Q17: So, if they're importing all the jobs from the Goodyear and Goodrich so making like we're still making tires with benzene and not here that means we're exporting more... they have more likely for them to get the MDS than we would?

Dr. Mikkael Sekeres: Well, this is the testimony in front of OSHA that put safeguards in place so that people wouldn't be exposed as much. So now in the US, you shouldn't be exposed as much, but if they don't have the same safeguards in Brazil, you're going to get it.

Q18: So in England. So besides exporting our jobs, we're exporting a disease.

Dr. Mikkael Sekeres: I mean, there are standards, the workplace standards.

So, how is MDS defined? I can draw this on the blackboard, but this is a prettier picture. So, I'm just going to look at this. In general, we think about it in terms of whether you have lower risk disease or higher risk disease. What do we mean by lower versus higher risk? The World Health

Organization classification is the standard for MDS and it divides MDS into a number of different categories, which honestly I would be disappointed in you if you had memorized, but you shouldn't waste any brain power on this. I have to waste the brainpower on this. They're descriptive based on what's going on within the bone marrow what the cells look like. So, refractory anemia means someone is anemic. Their red cells aren't working. Refractory and neutropenia means their white cells aren't working. Refractory thrombocytopenia means the platelets aren't working. You can have refractory anemia with ring sideroblasts which just means in their bone marrow you have cells look real pretty with rings around them. Refractory cytopenia with multilineage dysplasia which means you have a couple of cell lines that are involved. You might have anemia and low platelets or anemia and low white cells. Then you have refractory anemia with excess blasts. What are blasts?

Q19: Cancer cells.

Dr. Mikkael Sekeres: Cancer cells. That's a good guess.

Q20: Blasts are and I hope I'm right... They're immature cells like I had blasts and my white cells, gosh, they only live six days and they can't even make it. So, I'm a little disappointed in them. So, it's just immature cells.

Dr. Mikkael Sekeres: So, you're both right. Everyone in this room, myself included, has blasts in their bone marrow because they're immature white blood cells. In this diagram over here, blasts are at this stage. Maybe they're in second grade or third grade if you started out in kindergarten. So, we all have to have blasts to make normal white blood cells. Blasts become abnormal and become potentially cancerous when there are more than five percent or more in the bone marrow. How does that happen? Well, what's happening is each step here a cell is maturing. An even occurs that stops that cell from maturing and just making a whole bunch of copies of second graders instead of letting it go all the way through to high school and you can imagine the second graders can't go out and work in a factory. They can't go out and make a living. So, we think of it as a "cancer" because you have excess growth of abnormal cells just like you would in the rest and they're impacting the function of normal tissue. You don't have normal production of the cells you need to go into the blood stream. So, I use the word cancer. I do it a little bit provocatively not to scare anybody, but to say that there are some types of Myelodysplastic Syndrome that are like cancer. The more blasts you have, the closer you get to leukemia. That could be blood cancer, but then some people have Myelodysplastic Syndrome where one of my patients once called it myelo displeasure syndrome. He got it. Your counts are a little bit low. You don't need therapy and I have been following patients for 12 years who fall into that category where I haven't treated them yet, but they have MDS for sure.

So, I use the word and you may see the word on the Internet. Just keep in mind that there are different flavors of cancer. There's oh my God cancer. We got to treat you next week and then there's yeah, you got cancer. We're just going to follow you and not do anything, but it kind of

fits the definition of excess growth of abnormal cells that encroaches on normal tissue. That is the definition of cancer. So, (inaudible 24:12). So with blasts, we divide it into refractory anemia with excess blasts one or two, one if you have five to nine percent blasts, two if you have 10 to 19 percent blasts and once you hit 20 percent blasts, you have acute myeloid leukemia. Now, there's a line in the sand. The difference between somebody who has 19 percent blasts or 21 percent blasts. Really, are you kidding me? How much coffee that pathologist had that morning in his counting or her counting. Not that big a difference. So, some of my patients do go from MDS to leukemia but not this oh, my God. You better go in the hospital and treat your leukemia is yeah, you slid over a random number that we defined. We took the disease we could have made the number 11 percent. In the past, we made it 30 percent. It really doesn't make that much of a difference, but the more blasts you have, the more your bone marrow is failing to use your (inaudible 25:07). There's MDS with an isolated chromosome 5 abnormality called deletion 5Q. This is only important because there's one drug that works really well. We'll talk about that in a second and then there's what I call the pathologist's friend, MDS unclassifiable. That's where it looks for all the world like MDS, but it doesn't fit into one of those other categories. Any questions about that?

So, this is more commonly what we use to talk about MDS. This is the International Prognostic Scoring System and it codifies what should be pretty obvious. If somebody comes into my office and that person has a high blast percentage, that person has poor risk cytogenetics which means they have a lot of chromosome abnormalities that have occurred with their MDS and that person has multiple cell lines that are down. So, they have low red, low white, low platelets. That person is not going to do as well long term and somebody who comes in with just a mild anemia, normal chromosomes and a low blast percentage and this is what we use essentially as a staging system in MDS. MDS is horrid. It's not like breast cancer. Breast cancer you can get along on stage two. I'm stage three. This means I get a pink ribbon. With MDS, we don't have a real formal staging system. So, people will tell you what stage you're on? I don't know. I have MDS. So, this is what we use to stage people and it doesn't mean it's spread versus not spread. You have to understand the biology of the disease of what's going on and that's why I spend so much time trying to go over what's going on in the bone marrow because to understand MDS, you got to understand what's going on in the bone marrow. MDS is one of the most complicated things somebody can have. It is the hardest to explain. It's the hardest to pronounce and our... how we stage somebody is based on some pretty complicated stuff. Questions on this? So, this is something everyone should ask your doctor what is my IPSS score or there's a revised version. What's my revised IPSS? Yeah.

Q21: What is the median survival? What does that mean?

Dr. Mikkael Sekeres: Okay. So, that also is up there provocatively. If you go online you will see something about median survival. This system was developed before there were any drugs to treat MDS. This system was developed before there were decent antibiotics to treat infections people with MDS get. This system was published in 1997 and it was based on data from the '80s.

This is a rate and error system to be honest. So, it's not that accurate for predicting survival. So, median survival means average survival. That means as many people live a lot longer and there's many people live a lot shorter than that, but this is based on data from the 1980s. Ninety-three percent of people included in this system were never treated with anything. Can I have a show of hands of people that have never been treated with anything? Yeah. Exactly.

Q22: When you talk about the median, this drives me crazy because I'm down there and my doctor is like you're healthy except for this one little problem you have and why haven't they done new studies or are there any studies now that they're looking at with people with MDS because like you said that's from 1997.

Dr. Mikkael Sekeres: It's misleading. So, there are new studies. Let me see if I have... but with new becomes complicated. So, this is the revised IPSS. We were one of two centers in North America to contribute data to this. Now, you have a system that's based on criteria that are complicated enough that I actually have this taped up in the work room upstairs, so I can look at it before I go into a patient's room. This is based much more on the cytogenetics. Cytogenetics are the chromosome abnormalities that are in the MDS. So remember I said over here this stem cell starts out with a genetic abnormality. That's a chromosome abnormality and we have systems for determining whether it's a very good risk abnormality, a good risk, an intermediate, a poor or a very poor risk abnormality. Now, that classification spans about 25 different cytogenetic abnormalities. Twenty-five different chromosomal abnormalities and that's why I can't memorize it anymore. So, I have a list of what they are in my workroom, so I can start to classify people. This system also breaks down the percentage of blasts more than the other one. It breaks out the degree of anemia, the degree of low platelets and has a dividing point for the white cells... how low the white cells are. So yeah, we've gotten more sophisticated about it finally and this is a better system than the IPSS and this divides it out more. So, your score may be different on this system than it was on the IPSS and I have patients who go up or down on this system depending on how we do it. Now, this system also was developed in people who were never treated for their MDS. So, the difference in this system is just based on data from 800 MDS patients from around the world from the 1980s. This system is based on data on over 7,000 MDS patients from around the world, but still untreated because in developing the system the organizers of this and you have to understand this is politics like anything else. These are folks trying to organize across multiple countries around the world, wanted it to be as pure a system as possible so not have patients treated. Now, this has since been validated in people who have been treated, but only in isolated ways and it's not as accurate once you can treat it. So, it's a goof isn't it? Because it doesn't line up with how people are actually treated in the US, but this wasn't a US system. It's an international system and there are a lot of countries around the world where people with MDS aren't treated. So again, we have done some of the work in validating this, but what we've been doing is now increasingly incorporating more and more genetic abnormalities and making it a better system, but as we do that you can no longer memorize that this is something you have to plug data into an algorithm and have it spit out a score. So, we've gotten there. We're much more sophisticated, but now it's become almost impossible to say to

somebody figure it out on your own. You can't. I can't figure it out on my anymore. I've got to plug these genetic stuff into an equation that's weighted by how important each thing is. So now, you're multiplying something by .4 and something 1.2. It gets a little nutty.

If you're trying to simplify it and this is what I do. This is how I would classify the lower risk and this is how I would classify higher risk. Higher risk either has excess blasts or evolved into one of those higher risk categories and the IPSS or revised IPSS and lower risk doesn't have excess blasts and falls into one of the lower categories.

So, I'm not going to get into too much detail on this. These are some of the studies I talked to you about that showed the mutations in normal population of people who don't have MDS. So, this is that data from people who have schizophrenia and it just shows that over time as you age you get more of these abnormalities that may or may not develop in MDS. One of those abnormalities is called DMT3A. That's probably the most frequently mutated one. Again, this is just a normal... population of people with schizophrenia. There was another study done in a population of people with diabetes. Most people only had one mutation and just that it increases the likelihood of getting MDS or another blood or bone marrow disorder over time. The other really fascinating thing is that if you have these abnormalities, it's more associated with heart disease and there's going to be some research coming out essentially show that having one of these MDS abnormalities is more predictive of heart disease than high cholesterol. Crazy, huh? So, we have separately validated that here at Cleveland Clinic. We looked at everyone who's undergone a cardiac procedure here at Cleveland Clinic. We did about 25,000 people and found that there was a higher risk of having MDS and other bone marrow failure disorders in those folks than you would have predicted by the population. So, we've done the opposite. We worked backwards to show the same thing.

So, how do we treat lower risk disease? A couple of different ways. There's the... my favorite is the watch and wait. This is the Myelodysplasia Syndrome. (Inaudible 34:40) mild blood abnormalities. You don't need transfusions. You've got a good quality of life. These are folks I follow every one to six months depending on how well I know them and don't do anything. It's a social visit. We talk about grandkids and I've had these social visits with some people as I said for 12 years. I've only been here 13 years. That's my favorite type. Then you have some people who have an isolated anemia. One of the first things we will do is start what's called an erythropoiesis stimulating agent. That's either Procrit or Aranesp or Erythropoietin or Darbepoetin. These are hormones that stimulate the bone marrow and make more red blood cells. It's not chemotherapy. It's a hormone. The same hormone that people who have kidney failure get because the kidneys are actually the organ that makes erythropoietin in your body. They're the organ that sends anemia. So, we're giving people with MDS more of that hormone to stimulate more red blood cell production. For people who have that chromosome 5 abnormality we will start the drug Lenalidomide which is also known as Revlimid and in those people it works about two-thirds of the time. I think I had a slide on that later on. For people who have a low platelet count, we might start what's thrombopoietin agonist. These are drugs like Nplate or

Eltrombopag and these stimulate platelet production in the bone marrow just like Erythropoietin stimulates red blood cell production in the bone marrow. It's a growth hormone. It's not a form of chemotherapy. We will also use things like antithymocyte globulin. What the heck is that? There's a theory in MDS that some of them get this caused by the immune system attacking the bone marrow. So, what we do is give a drug that stops immune system from attacking the bone marrow and allow the bone marrow to grow normally. It works about 40 percent of the time and it's the same drug we give to people who have something called aplastic anemia which is a total wipe out of the bone marrow or we'll use the hypomethylating agents. What are those? Those are the drugs like Vidaza or Dacogen and sometimes we'll give those to folks with lower risk MDS though we usually save that for people who have higher risk MDS.

Q23: What about people with the low white blood count?

Dr. Mikkael Sekeres: You are very insightful because we deliberately left this off of this chart. We got a little bit of flak for that. This was published in our big society, the American Society of Hematology, and we have an annual meeting in December of every year. So, the worst time in the world to get sick with your MDS is the second week in December because we're all at this meeting. There's education book that's published each year. So, this was the section that Holly and I wrote for this education book and we did not include that because there are no data supporting use of growth factors to boost the white cells in somebody with MDS. There has never been a good study that's been conducted. My personal theory is what it's doing is raising the number and it must feel good that the number is raised, but I don't think it actually improves the immune system. So, it is used by people. It's not the wrong thing to use though. My personal... My assistant (inaudible 38:07) use it, so we didn't include in this algorithm.

Q23: So, people with the white blood, it's not allowed to treat them?

Dr. Mikkael Sekeres: Antibiotics. If they start to get infections. You can give this shot, Neupogen or Neulasta are the two shots that are manufactured. It will make a white count higher. I've never been convinced that's more than just an improvement in number. I've never been convinced that actually improves the immune function. That's my bias.

Q24: Is that true with Vidaza? As the number goes up, being treated with Vidaza do you think that it's likely that just the change in the number and not a change in the immune system?

Dr. Mikkael Sekeres: Great question. With Vidaza it's not just a growth factor. With Vidaza it actually changing the dysplastic cells. It's actually working on the source. So in that case, I think it is working. With the growth factor, I think it's just boosting up the number.

Q25: But they use Vidaza for low... if the whites get low, they start using Vidaza.

Dr. Mikkael Sekeres: Absolutely and if that's the case and it's Vidaza that's being given and if the whites improve, I think that's real. I think then you really do have more bone marrow function, more bone marrow production as opposed to just squeezing the cells to make more.

Q26: I was at an appointment with my father and when we mentioned the white blood cell line because his is that way as well, they said that they thought Neulasta perhaps would raise the blast count too, not just raise the white blood cells.

Dr. Mikkael Sekeres: Great point. So, I don't use growth factors in somebody who has excess blasts. So if a low blast percentage, two to three percent, which is probably what I have. I think it's fine to use. Once you get up to five percent, I stay away from them because the blasts have receptors on them for growth factors. So, I avoid them in that sense. There was one study that was conducted in 1993 and published in abstract form where Neupogen was given to people who had excess blasts with MDS and it showed a higher rate of them evolve into leukemia. That study was never published in final form because the drug companies divested. So, I don't use (inaudible 40:23). Thank you for pointing that out.

This is a study that just came out at our annual meeting of that Revlimid drug. Now Revlimid is FDA approved for people who have that chromosome 5 abnormality and in those people it works about two-thirds of the time meaning that if you require a blood transfusion every two weeks, one week, three weeks and we treat you with this drug, two-thirds of the people will no longer require a blood transfusion for a while. So, that's as good as it gets for us by the way. That's a really good what we call a response rate, but it's not permanent. It doesn't fix it. On average people go about two years without needing a transfusion and then they start to need transfusions again, but only about five percent of people with MDS have that chromosome 5 abnormality. So, what about the other 95 percent? Well, this was a study that looked at the other 95 percent of people who don't have that chromosome 5 abnormality, but who have lower risk disease and it was a randomized study conducted in Europe where people were randomized. So, they either got the drug Lenalidomide, Revlimid or they got placebo and then they were followed over time for whether or not they started to no longer need blood transfusions and what this study found is of people treated with the drug Lenalidomide about 27 percent achieved what's called a transfusion independence, red blood cell transfusion independence lasting eight weeks or more, 27 percent. Remember, it was 67 percent in people who had their chromosome 5 abnormality and those who don't 27 percent and that's pretty typical of someone with lower risk MDS to be treated with the drug. If they started to get that transfusion independence, 90 percent of them got it within four courses of therapy, about four months of therapy. So one of the teaching points with this is don't give up too soon. If you're on the drug for two months for MDS, it's not long enough. For lower risk MDS, you got to stay on the drug for four months before you declare victory or defeat. For someone with higher risk MDS, it's six months. So, don't give up too soon. A lot of referrals I get for patients are this person was on this drug and the drug didn't work and well they were only it for two months. That's not enough. So, I encourage them to go back on it for another four

months and see what happens and sometimes it'll work. Sometimes it won't and they come back to me then we come up with something else to do, but don't give up too soon.

Q27: So, is this drug normally given after like injections with your red cell and so on and not before?

Dr. Mikkael Sekeres: Yeah. So, it depends. Most people I see with MDS with lower risk disease, so not the ones who have the excess blasts, not the ones in the high categories of the IPSS I'll start out with either Procrit or Aranesp. So, you give the growth factor because you know it ain't chemo and it has about a 40 percent chance of working. So, I find that first and I try for four months. Don't give up too soon. If it doesn't work by that point and I do increase the dose in the middle then I will go for this drug.

Q27: And is there one that's better than the other, Aranesp or Procrit or can you alternate because that's what happened with me. I came up to Illinois and they didn't have Aranesp so they started using Procrit.

Dr. Mikkael Sekeres: Either is fine. So, we've done some of these studies and also we participate in any studies. Neither is better than the other. It's a matter of contracting. Sometimes there's contracts with Ortho Biotech which makes Procrit. Some contracts with Amgen which makes Aranesp.

Q27: And yet they're... research said that it lasts a little longer between and you don't have to get the shots quite as often.

Dr. Mikkael Sekeres: It's (inaudible 44:32) difference. Aranesp you can get a shot as infrequently as every three weeks. Procrit you need it every week.

Q27: Really?

Dr. Mikkael Sekeres: Yup.

Q27: Because they said 600 some units or something... they doubled the amount of Aranesp and they're only getting it every two weeks.

Dr. Mikkael Sekeres: Certainly, Aranesp can be as infrequently as three weeks. So, it can be two weeks. Procrit is measured in more like 60,000 units and that has to be weekly, but neither is better than the other. It's just the frequency issue.

The duration of response, remember I said it was two years for people who have the chromosome 5 abnormality for those who don't have the abnormality the duration of response is about 33 weeks. So, it's a lot shorter also. I have certainly had folks on this drug who gone two

years without a transfusion when they didn't have the chromosome 5 abnormality, but the average is about 33 weeks. So, it doesn't work quite as well in this group of folks, but it's worth a try because if it does work then everyone wins and it's a pill.

There's a new drug that's being studied. In the US we have a drug called Sotatercept. In Europe its Luspatercept and I think the company is going to be moving forward with this drug rather than the Sotatercept. They work about the same though. These are drugs that are somewhere in between a growth factor and a type of chemotherapy. In this study, I'm just going to kind of go to the bottom line here. The overall response rate was 41 percent. So, 41 percent of patients treated on this started out needing transfusions, red blood cell transfusions, and then didn't need a transfusion after being treated with this drug. In the US study, the Sotatercept which is here, the response rate was 42 percent. So, you start to see in different continents the exact same response rate with drugs that are almost identical. You start to believe it. They're validating each other. So, we're seeing decent response rates with this drug. It is going to move to a phase three study which is going to try to go for FDA approval. They've gotten a good buy in from FDA and from the European Union regulatory agencies. We have this drug on a clinical trial here, the Sotatercept. We will have the Luspatercept once it opens. It's going to open in a few months and this is also why I'm encouraging people who are in this category of anemia, lower risk MDS, have tried Procrit and Aranesp, maybe have tried the Lenalidomide, I'm offering them this study. I think this is probably the drug with the highest likelihood of getting FDA approval next in MDS.

Q28: Is it an injection?

Dr. Mikkael Sekeres: It is, about every three weeks.

Q28: It's a week injection.

Dr. Mikkael Sekeres: Yup. So, same as Aranesp. Every three weeks.

Okay. What about folks who have low platelet counts? So, this was a study we participated in as well. It was a randomized study where people got either Nplate Romiplostim or a placebo and were followed over time to see whether the Romiplostim improved their platelet counts or it decreased a number of bleeding episodes they had. In this study the drug was significantly likely to reduce the platelet transfusion, the number of platelets people received. For those who got the Romiplostim Nplate versus placebo and significantly reduced the number of clinically significant bleeding events for those who got Romiplostim versus placebo. Well, looks like a winner. Right? Well, the funny thing happened on the way to the forum with this one. Remember the question that you asked about whether these drugs would be given to somebody with excess blasts. In this study, we said don't enroll patients who have excess blasts for this study because this will stimulate their blast and increase and you will see more episodes of people getting leukemia and the company got greedy and said, "Well, if we don't, it's going to take us forever to enroll for

this study and that's going to cost us a lot of money. So, we're going to enroll them." This is how things happen. So, indeed, what happened at the end of this study they looked and there was significantly higher number of people who were treated with the Romiplostim who went into leukemia than those who didn't. So, the study was stopped prematurely. Over time, it's been followed up and those rates five percent versus six percent evened out and if you look at this graph of this is called Leukemia 3 Survival. So, you see these lines are overlapping. So, it looks like over time it may have just been an early quirk and there didn't appear to be higher rates of people evolving into leukemia because of the drug. I think what the drug really did is increase the blast percentage transiently and then the drug was stopped and it went back down, but because of this I will venture to say I don't think you will ever see this drug specifically approved for MDS because now the FDA is going to say, well if you want to be approved for MDS, prove to us that it doesn't cause leukemia and that's going to be too hard a study to design. So, do I give this drug to my MDS patients? I do if they don't have excess blasts and after we have 15 minutes discussion about their risks and the result of this study and if my patients are comfortable with that and I am comfortable giving this to people who don't have excess blasts, but getting insurance to pay for it and also going over risks with somebody God forbid that person does evolve to leukemia. Was it the drug I gave them or was it going to happen naturally? Probably would have happened naturally if they don't start out with excess blasts, but I don't know for sure. So, this is out there. I give it myself, but not to people with excess blasts.

So, what about higher risk disease? Well, this is a bit of a complicated algorithm that talks about a transplant versus not transplant. If somebody has higher risk disease, I always have a discussion with that person about getting the bone marrow transplant. We transplanted people with MDS up to the age of 75 here and we always say there's no age limit to it. It is the only cure for MDS, not for someone with higher risk MDS. There have been some studies conducted that have shown that transplanting early in somebody with higher risk MDS leads to better survival. So, I always talk about it with my patients. It's not the easiest thing in the world if you have somebody whose 74 who may have heart disease whose siblings that may be donors may themselves have significant disease. They may not be able to get a bone marrow transplant and that's probably true with the majority of folks, but we still talk about it and offer it and I do have a decent percentage of my patients go on to get a transplant.

Q29: Do they have any statistics on the survival rate with the transplant and MDS. I mean, somebody with like more than... you'd rethink like two, three years, five years.

Dr. Mikkael Sekeres: Oh, yeah. Sure. These folks were cured, cured of their MDS with the transplant. Absolutely. One hundred percent that happens. The percentage of people who...

Q29: (inaudible 52:17) cured and then let's say that their normal lifespan would have been additional 15 years. They got the transplant and they're cured. Would their normal lifespan barring anything else, 15 years then? Have you seen long term?

Dr. Mikkael Sekeres: We have seen long term. If you look at population based studies, people who get a transplant do not live as long as (inaudible 52:43) controls who didn't have MDS, didn't have cancer, didn't undergo a transplant, but when we say cure, they don't die of MDS. They don't die of cancer. They die of something else. So, I always say to my patients get the transplant. I hope you're cured and you still got to look both ways when your cross (inaudible 53:03).

Q29: Go around those yellow lights.

Dr. Mikkael Sekeres: Advice I should take more often. So, that's the only cure. Most people don't get one, so what we do is we start what's called one of the hypomethylating agents. So, either Azacitidine, Vidaza, Decitabine/Dacogen. Azacitidine is the only drug to have been shown to prolong survival in people with higher risk MDS. This is a European study where people were randomized to getting Vidaza, Azacitidine or a conventional care regimen. Most of them get that supportive care. So, blood transfusions, antibiotics, but nothing else. In this study, 15... the median survival... that's that median survival you talked about before. There's 24 (inaudible 53:50) hormones for those treated with the Azacitidine and Vidaza and 15 months for those who didn't get the Vidaza and that was the significant difference. This is the only study that shows survival of managing people with MDS.

Q30: Do you get your patients that have... that their blasts keep going up. Is it someone that you would look at for a transplant eventually or (inaudible 54:12) so then the other forms of MDS?

Dr. Mikkael Sekeres: The studies that showed a survival advantage to transplanting early were done based on IPSS. So, they were done based on whether you have a higher risk MDS by the IPSS. Now, there had been an attempt to revise those based on the revised IPSS and it still works. So, they're higher risk by the revised IPSS we would do them, too, but they don't look purely at blasts. It also incorporates the chromosomes and the number of blood counts that are affected.

Q31: On the transplant, would you do one of those new kind of reduced intensity or haplo... haploids or (inaudible 54:53)?

Dr. Mikkael Sekeres: Sure. So in general, there's no line in the sand with this. You have a 62 year old who's out playing tennis every day and is competing in the senior Olympics. That person may get a fully ablative transplant. In general if you're under 60, you'll get a fully ablative transplant, over 60 you'll get a reduced intensity transplant. So, we call it reduced intensity. There is nothing reduced about the (inaudible 55:21) of the transplant though. It just that you get it at an outpatient. You don't get as much chemo upfront.

Q32: What's the oldest person you've ever done? Seventy-five is the oldest?

Dr. Mikkael Sekeres: Seventy-five. Seventy-five that I know of. There may older in our bone marrow content database. Seventy-five year old in my patients.

Q32: Is that with the full blown transplant?

Dr. Mikkael Sekeres: No, he got the reduced intensity.

Q32: And what's the survival rate? Is that much lower than with reduced intensity or is it still considered cured?

Dr. Mikkael Sekeres: Those who are cured are cured. The outcome is the same whether you get the reduced intensity or the full transplant.

Q32: Another question regarding transplants. If you don't have a donor match, 25 siblings what the heck are they doing, but they're not a match. What about blood cord? Do you use blood cord?

Dr. Mikkael Sekeres: So, what our (inaudible 56:12) folks will do is they'll first look at siblings and see whether you have a match from the sibling. Next, they will look at the same time at the National (inaudible 56:19) Donor Program for umbilical cords and see where the best match is. If they can't find a decent match there, then they will go to what are called haplo identical which are half matches. So, you might get a transplant from a child, for example, but those are... you're taking increasing risk with each of those approaches.

Q32: But if you had full match with blood cord then that should be as good as a sibling.

Dr. Mikkael Sekeres: If it's full match is a bit of a rolling number. You'd have a six full match, a 10 full match, a 12 full match. So, the absolute highest full match if it's the same if it's a full 100 percent 12 out of 12 then your outcome will be about the same as if you got it from a sibling. I would say somewhere out there you have a brother from another mother. I didn't say father. That happens also.

Q33: With the reduced intensity transplant is just as good as the other, why would you gamble and use the other?

Dr. Mikkael Sekeres: There are some nuances of the two that are different. So and you're getting a little bit out of my wheelhouse of expertise because I'm not a transplanter, but there are different weights of graft versus host disease between the two and I think my Spidey-sense tells me that transplants are still think that the fully ablative one is better even though the data don't support it. So, I feel they push toward that if they can, but the data says that the outcome is the same.

Q34: Question. I was diagnosed with MDS/MPN in April of this year, going through... I'm finished my fourth cycle of Dacogen. I've also they've identified six to seven bone marrow matches for a transplant. I'm 68. How do I make the decision or whatever you look at as far as like the plus/minuses of continuing with the Dacogen versus pursuing a transplant?

Dr. Mikkael Sekeres: You have another three hours? It's a very hard decision and it's a personal one. I was telling the story earlier. My uncle had leukemia and was treated at University of Chicago and actually cared for by our next speaker and he was debating whether or not get a transplant for his leukemia. So, I gave him my most neutral perspective on the face of the Earth. He could not get me to commit to one side versus the other perspective on it and at the end he said to me, "Well, I decided to go for the transplant even though you were so negative about it." I wasn't, but he looked at anything that wasn't absolutely positive as being negative because his bias was to go for the transplant and I couldn't speak for him. So, it depends on your personality with it. If you started out... and MDS/MPN overlap... it's very complicated. It's one of my... personally one of my favorite topics that I love the complexity of it. We really specialize in it here. We've done a lot of the work to define the biology of that here and there are very few clinical studies of what to do with folks like you because you, sir, are a rare duck doc and a lovely duck, but a rare one all the same. So as a result, it's very hard to get drug companies to commit to doing the study just in people who have overlap disorder. So, I and colleagues are trying to push them to do that so we now... we actually conducted the very first study in people with overlap disorder. The very first clinical trial was done here. There's another study that's ongoing with... We have an MDS Consortium, us and five other sites around the country where we're doing this study of the drug Ruxolitinib in people who have overlap disorders. The brand name is Jakafi. It's approved for people who have myeloproliferative disorder. So, we're using it in overlap. We've a follow up study we're about to do just in people with overlap disorders. So, there's very little research out there about this and there's very little research in transplanting people with overlap disorders. So, we tend to beg, borrow and steal from the literature with MDS for people like you and say, well, if it works here it should work for you, too, and for the most part that's true. So if your doctors at the outset recommended a transplant the best time to get that transplant is when you're doing well on a drug like Dacogen because once the Dacogen stops working your MDS/MPN overlap is going to be coming back and harder to control in time for the transplant because we don't have great backups behind Dacogen and Vidaza. The drug that we were hoping would be the backup drug is right now had a negative study. It failed. So, while you're on the stuff that's working that's good. The best time would go for it personally, but I'm speaking to you from the perspective of somebody who has young kids and has led a very different life than you.

Q34: What are you talking about with overlap disorders?

Dr. Mikkael Sekeres: So, some folks have Myelodysplastic Syndrome and something else called a myeloproliferative neoplasm, an MPN. They have it at the same time and the longer my patients are living the more I'm seeing it in people. They'll start out with MDS and they start to

get the MPN or they'll start up with a MPN and start to get the MDS. Think of it... I'm going to reflect back what (Attendee), I hope I use your first name. What (Attendee) said earlier it's a bone marrow failure condition and there are other bone marrow failure conditions that can overlap depending on what genetically happens with it.

Q34: They test projection mutations in this MPN/MDS overlap?

Dr. Mikkael Sekeres: I don't because it doesn't change my therapy.

Q34: Do we want to... If you had that wouldn't you want to relax (inaudible 1:02:36) assuming that helped?

Dr. Mikkael Sekeres: Ruxolitinib works in patients irrespective of their JAK2 status. So, they named it Jakafi, but that's a misnomer.

Q34: Oh, okay.

Dr. Mikkael Sekeres: It's one of those drugs that was developed based on the biology, but then it turns out people it was working in had nothing to with the biology they thought it was. Welcome to (inaudible 1:02:57). That's 90 percent of the drugs we use are by accident.

Q34: Thank you. I appreciate it.

Q34: So, what did your uncle decide to do and what were the results of...

Dr. Mikkael Sekeres: Well, he went for a transplant at the age of 72 and unfortunately he died of an infection afterwards. He had outstanding care at the University of Chicago and I, obviously, had asked if they got him into the best people in the world, but it was... I can honestly say it was his decision to see if I was being negative about it, but there are people who die. There's a mortality associated with transplants.

Q34: Did he die right after the transplant or did he have some remission for...?

Dr. Mikkael Sekeres: He had remission for a while. He died probably about six or eight months afterwards.

Q34: I just know of a man, the same principle. I think he's pretty good for about 10 months and then reverted and died.

Dr. Mikkael Sekeres: But I know people who were cured also. Everyone's different. One person (inaudible 1:04:02) on another person.

I'm going to have to wrap up because I'm 15 minutes over which I'm embarrassed about. I don't want to keep everyone else. This is the study with Dacogen and this is the drug that you're on. I put this out there because you may or may not know about this and I want to put it in context. So, this is a similar study to what I just showed you with the Vidaza, but in this study there was no survival advantage for Dacogen versus best supportive care. Now, those of us in the community think that this is crazy because these drugs are identical ones actually converted to the other in the body and what we think happened is that the folks who designed this study screwed up and in fact they have a history of screwing up studies. So, I don't think there's any difference really between Dacogen and Vidaza and you can tell they screwed up because look at the comparison group. The comparison group here lived 10 months. The comparison group here lived 15 months. That can't be the same population. Right? So, this group had a failing study. The Vidaza study was the only one to show a survival advantage. I'm comfortable with either drug being used. I don't think there's any difference between them, but I just throw this out there so at least you've heard about it.

In terms of new drugs... I'll go through this very quickly. There's a new drug that's a version of Vidaza and Dacogen called SGI110. This is entering advanced phased studies. In these studies, people who are a response rate in folks who were previously treated with Vidaza or Dacogen this is a little bit of a lie. It's not 23 percent but they included what's called a marrow CR here which isn't a real response, true response rate. It's probably closer to 10 percent. For those who had never been treated with Vidaza or Dacogen, the overall response rate was about... subtract this out again, so about 32 percent, 33 percent and that's exactly what the response rate is for Vidaza or Dacogen. So, I think this is going to be a similar version of the other drugs, but I believe this is given as a pill. So, you'll have a pill version of Vidaza and Dacogen.

We've done some studies when we add drugs together. This has become the old commercial you got your peanut butter in my chocolate, you got my chocolate in your peanut butter and we made Reese's Peanut Butter Cups. So, do we make Reese's Peanut Butter Cups when we add two drugs together? We don't know. This is a large study. I was the lead investigator across North America where we randomized people getting Vidaza or Vidaza plus Revlimid or Vidaza plus another drug called Vorinostat. In this trial, slightly more side effects for a combination of drugs, but not a huge number of more side effects for a combination of drugs. More rash in the folks who got Revlimid, more GI problems in those who got Vorinostat. The overall response rate... these numbers have actually changed its 37 percent for Vidaza, 45 percent now for this combination and 24 percent for this combination. So, slightly higher response rate for this for Vidaza plus Revlimid versus Vidaza alone, but not significantly higher. What we have found though and this has actually held out really nicely is that in folks who have overlap disorders, this is chronic myelomonocytic leukemia. There are a now... is a significantly higher response rate for the combination of Vidaza and Revlimid. So for you because I'm really interested in people like you. So, we deliberately enroll people like you into this study. There may be a slightly higher response rate for (inaudible) with that, but I cannot say that having two drugs is better than one right now. This is still an unresolved question. We're still analyzing the data.

This was the drug we were hoping would be available for people who were exposed to Vidaza and Dacogen. Three hundred people were enrolled into this study across the world and in this study the survival was slightly higher for those who got this drug, Rigosertib at 8.2 months versus about six months for those who got best supportive care, but this was not a significant difference. So, the fate of this drug is unclear. It didn't meet its benchmark. It didn't do well enough to get FDA approval. So, they're thinking about designing another study looking at a slightly different population, but we don't have our stager yet and that's why for somebody like you I would think (inaudible 1:08:34) transplant while the Dacogen is working.

So to wrap it all up, the molecular genetic landscape of MDS is becoming much more complex and it is now being folded into clinical prognosis schemes like the IPSS or IPPS-R therapy for low risk disease, addresses specific cytopenias, specifically anemia. For higher risk disease, it is hypomethylating agent (inaudible 1:09:03) therapy. We have more data coming with combinations and an excellent regulatory frontier in the relapse refractory setting for lower and higher risk MDS.

So, I want to thank all of your for coming today. I always thank our team... this... we even have more people that this right now. It really takes a village to have an MDS and leukemia program. I'd like to thank you all.

Q35: I don't want to run you over. Could you explain what the SF3B1 mutation is.

Dr. Mikkael Sekeres: Sure. The SF3B1 mutation is what's called a splice cell mutation. We started looking at genetic mutations just in the chromosomes. So, your first glance is just chromosomes. We each have 23 pairs of chromosomes, so 46 chromosomes that are looked at and literally people take... they grow them, take a photograph of them and then look and see whether they look normal or not and if there are abnormalities they'll say, oh, you're missing part of chromosome 5 or something like that. Within each chromosome are thousands and thousands of genes. So, then we started to look not only at chromosomes that those genes that make a cell grow badly or grow too much but also that are involved in other mechanics within of how a cell functions. One of those mechanics that when genes copy themselves they have to be cut. So, the cutting is done by what are called splice (inaudible 1:10:40) and some mutations are in those things that cut and they don't cut well to make copies of those chromosomes. The cell is incredibly complex. So, the SF3B1 mutation, that cutting mutation, it's called a splice (inaudible 1:10:54) mutation has been found to be almost diagnostic of that (inaudible 1:10:59) ring sideroblasts when you see those beautiful rings around them. Ninety percent of those people have an SF3B1 mutation or some other splice cell mutation.

Q35: Does that change any part of the risk factor or your scoring?

Dr. Mikkael Sekeres: Another great question. So, there's a lot of controversy about this at first. We published data where we said folks who have this mutation do much better. Mayo Clinic published data where they said people who have this mutation don't do better or worse. It's neutral. Dana Farber published data saying that they did better. So, we want to combine data and overall I can now get at those who have that mutation do better, they live longer. Well, we're looking at now is whether people who have that mutation can have a drug designed specifically for it and there is a company called H3 Biosciences which is designing a drug specifically for this.

Q36: Which mutation is this?

Dr. Mikkael Sekeres: It's called the SF3B1, SF3B1. That's the Holy Grail is that you got all this stuff about Obama mentioned precision medicine at the State of the Union address and there are a few hundred million dollars being allotted for studies of precision medicine through the National Cancer Institute and the NIH. That's our goal is that we'll be able to identify these genetic abnormalities that lead to specific drug therapies and we're getting there, but it's slow. We're not there yet. That was a great question. I'm glad you asked that.

Q37: Have you ever heard of medication... if I pronounce it right Blincyto for high risk and would it work?

Dr. Mikkael Sekeres: So, Blincyto has been FDA approved for ALL, acute lymphoblastic leukemia. That's the long name of its lineage (inaudible 1:12:52). That's a tongue twister and what it does is a (inaudible 1:12:56) antibody. So, on the outside cells are proteins that are like bar codes that define what kind of cell that is. This drug latches onto this bar code on this leukemia cell and then destroys it and it works really well in people who have acute lymphoblastic leukemia that's come back as relapsed or that's refracted and never went into remission. So, we're using this in patients like this to try to get them to a bone marrow transplant which is there curative therapy. It hasn't been engineered for people with MDS. Now, we are looking at something... It's called a monoclonal antibody, that class of drugs, monoclonal antibodies. We're looking at a different monoclonal antibody in MDS that we have available right now that targets a different protein on MDS cells. So, we're looking at that direction and this is more complicated than the leukemia is.

Q38: I know you're trying to get out of here...

Dr. Mikkael Sekeres: My time is irrelevant. I'm worried about their time and your time.

Q38: ... I was wondering if you were familiar with... I read something about John Hopkins chemo cancer center developing a tumor vaccine to boost immune systems of MDS patients and improve bone marrow function.

Dr. Mikkael Sekeres: So, there are a lot of different approaches to treating disorders like MDS or cancers and there are some that have been like the Holy Grail like vaccine therapy or trying to reigning in the immune system to attack the bad stuff and if you saw the Ken Burns Cancer special that was on PBS in end of March beginning of April they talk about this a little bit. The theory is that if you take bad cells out of a person's body and that person's... Let me start with the vaccine therapy. The theory with vaccine therapy is that you can take the bad cells out of somebody's body, develop a vaccine specifically for those bad cells and then give that vaccine to somebody, give it back to that person. It's a real interesting cellular engineering that's going on. Very person specific. You can imagine what this costs per person to do this sort of stuff, right. So, that has been tried in some leukemias and has worked in a few people. We have these like miracles responses. Maybe doing clinical studies like this investigators will always say it's always the first person that does the best. They do the best and they think they're like oh, my God. My career in doing this. This is the holy realm and it doesn't work in the next 30 people and that's what happened with some of the vaccine therapies for leukemia. It worked on the first couple people. Everyone said oh, my God. This is the future and then it just didn't work in most people. So, they are developing those. They're highly experimental. I haven't heard a lot of success in MDS yet. The other one is trying to commander the immune system and we are going to be coming online with a study.

Q39: Is that like T cell modification.

Dr. Mikkael Sekeres: Yeah. So, they're CAR T cell story. We are going to have a CAR T cell protocol open here that really works better with people with lymphoid malignancies, acute lymphoblastic leukemia, chronic lymphocytic leukemia. You heard the story about the kids with leukemia at Penn where it was used. Right? We are kind of in line with those trials. We'll look at that in the next couple of months. Then there's the immune checkpoint story and this is the one where you've heard there these melanoma growths that have come out that have revolutionized the treatment of melanoma and these folks who were on Gator (sp?) somebody like Oliver Stacks who has... I don't know if you know Oliver Stacks the physician (inaudible 1:16:45) metastatic melanoma now. They got responses in like 60 percent of these people. So, it turned out they also work in lung cancer. There's a big presentation on the American Society of Clinical Oncology in May that showed that. We are looking at it in MDS. We don't even have a lot of preliminary data on how effective it is yet, but we are going to have a trial open here where we're going to combine one of those checkpoint inhibitors with Vidaza and that will come online in about six months.

Thanks everyone for staying awake and paying attention.

(Applause)

Q40: (inaudible 1:17:37) you get a gold star for explanations.

Dr. Mikkael Sekeres: My parents were both English majors and they promised they would knock me upside the head if I ever used lowly doctor speak.

Q41: We appreciate it.

Q40: We really do. We went to the forum in Columbus and thought Jane was absolutely excellent just like you, but the doctor was on top of his game, but he couldn't tell us in our terms. You've done a great job.

Dr. Mikkael Sekeres: Oh, thank you. Thanks.

Q41: If this was your white chalk take, how much different was your fellow's talk?

Dr. Mikkael Sekeres: Honestly, not that different because you speak English you could be able to speak English to any crowd. That's always been my philosophy. It's probably flawed, but so it's honestly not that different. I quizzed the fellows and used the same language.

Q41: I could see this could be almost the same one. Same also getting them up to speed. (inaudible 1:18:37) Thank you.

Dr. Mikkael Sekeres: No, thank you. Thanks much for listening.

Jean Ridgeway: So, (inaudible 1:18:56) luncheon. Take a little break, get up walk around a little bit and then (inaudible)

Is everybody ready to start the afternoon so we can finish up and get you out here in a timely fashion? I'm Jean Ridgeway and I happen to be a member of a nursing leadership board with the Myelodysplastic Foundation and I'm here to kind of just being the facilitator and the coordinator for this afternoon, but hopefully it's a continuation of this morning and much like Dr. Sekeres and relatively informal. So, we have slides, but we don't have to go through them. We can use them as a talking point or whatever, but I think... so perhaps all of us can get a better understanding of why we're all here. It'd be nice to go around and introduce ourselves. Just let us know what you're here for. If there's something really specific that you're looking to get out of this afternoon, I think that would be helpful for me especially. So, but I do have to warn you that there are no filibusters allowed. You'll be promptly be escorted out. So, keep it short. Get your act together and let us know. So, I'll give you a little background on myself. I do live in Chicago. I work at the University of Chicago, so I work fulltime and I work as an advanced practice nurse. I am a nurse practitioner. For those of you who have seen me before since I've seen you last, I've finished my doctorate.

(Applause)

Probably not as glad as my husband who really had to carry the bulk of everything at home. So, I'm married to a great guy who retired and I have four children, one of them who is now a nurse practitioner. She works in the pediatric (inaudible 1:23:53). So, and I have worked with malignant hematology my 30 plus year career as a nurse practitioner. So, I feel well acquainted with some of the progress and the issues and have the privilege of working with malignant... folks who have malignant hematology problems on a daily basis. I also work about 50 percent of my time as we kind of cross the bridge from standard of care with MDS or leukemia and just stem cell transplant. So, I do half of my responsibilities really are with stem cell transplant and have found a niche with one of my physicians really working with "older patients" going through allogeneic stem cell transplants. So, we look at anybody over the age of 55 as "older" simply because of the biology of this disease and then oftentimes other illnesses that can be present in adult life, but we do transplant patients up into their 70s. So, it's an interesting journey. So anyway, that's who I am.

Q42: Success rate on people over 70.

Jean Ridgeway: You know, it really depends on is the patient really kind of pass the muster test. So not everybody that goes... we have an extensive evaluation clinic. It's called the TOP Clinic and it standards for The Optimization Clinic for Older Adults and it's a multi-disciplinary clinic. Folks meet with our transplant specialist. I meet with them. We have physical therapy, occupational therapy, nutritional services, social work. We have patients go through a pretty extensive what we consider neurocognitive testing. That's done with our colleagues in psychiatry. That takes about three to four hours. So, that's done before folks come to that. It's a half a day clinic and then when we're done we get together and provide some guidance towards the referring physician. So, we have a policy. When you work with your doctor there's this emotional ownership that takes place that sometimes does not allow people to be entirely objective and so a different oncologist, not their treating oncologist is evaluating them from a medical oncology perspective in that clinic. So to answer your question if people do go through transplant and they're over the age of 70, how well do they do? We make sure now that people are really kind of optimized. There are some people that have to go to through pre-physical therapy before we'll consider treating them, but if they're medically fit to go forward they do as well as any transplant patient. Infection still is a concern. We have to be really careful about infection, but I saw a couple people yesterday. One gentleman was 68, another guy he is 73, somebody else is 74. There like two months out of transplant. Tired. Really tired. Pretty common. So, they can do well.

Q43: I don't know if you know any of the financials, but once you're 65 and if you're on Medicare, Medicare does not cover bone marrow transplants. Does your hospital or your facility look at putting them into studies so it would be covered?

Jean Ridgeway: I don't know the answer to that. I will tell you this though that no one in our institution goes forward until the financial green light is given. So, what happens if someone...?

I'll just give you a bit of background. So, if we're considering you for a transplant we write a letter to your insurance company and we basically lay out the rationale of why we're considering the transplant and then they give us feedback. Either they approve or they deny. Sometimes insurance companies will say you can get your standard treatment at hospital A, but you have to go to hospital B for your transplant. That's with the contract. No one ever reads the fine print in their contract. Right? Your medical coverage until you read the last page and you need it.

Q43: I know that my health insurance right now would cover it, but when I turn 65 this year...

Jean Ridgeway: So, I don't have to deal with the financial piece, so I don't. We have a financial coordinator.

Q43: Yeah. I just wondered.

Jean Ridgeway: But nobody could afford it.

Q43: No, I know that.

Jean Ridgeway: Sometimes what the other issues that come up are just oral medications because there's so oral medicines that people go on after transplant. Anyway. Alright, so let's start with (Attendee). So, tell us who you are and where you're from and if there's something you want to know about today?

Q44: My name is (Attendee). I'm here today with my sister, (Attendee). Our father was diagnosed about...

Q45: June 23rd.

Jean Ridgeway: So, your dad was this year?

Q44: He's 89 years old.

Q45: After six years called him (inaudible 1:28:55). But he is too old even go for a mini transplant.

Jean Ridgeway: Yes, that's very true. But there are a lot of other options like we talked about this morning.

Q45: Yeah, he's doing Vidaza and it's just at the beginning. It's a big (inaudible 1:29:15). We're doing all we can to support him.

Jean Ridgeway: Great. We kind of know who you are.

Q45: Yeah. I'm (Attendee). I'm here with my brother for my father and trying to collect as much information as we can and to support him and my mom and just want to make sure we have all our Is dotted and Ts crossed.

Jean Ridgeway: Exactly. There are a couple extra binders outside, *The Building Blocks*, if you'd like to take another one or so back for a friend or for your son, feel free to do so. (Attendee)'s next.

Q46: (Attendee) and I was diagnosed in 2013 with 5Q- MDS and I'm just here to learn. Dr. Sekeres is my doctor.

Q47: (Attendee) and I was diagnosed August 15 of 2014 and I... my doctor, she said you have a funny one because I don't have... they classified me as RAEB 1, almost 2. I have excess blasts and low white count. So, otherwise I feel okay. My doctor, maybe you know her, Allison Walker, from Columbus.

Jean Ridgeway: And are you on treatment or not on treatment?

Q47: No and there's been... I have another bone biopsy next month and we'll see where we go from there. (Inaudible 1:30:55) keep going or go in a different direction.

Jean Ridgeway: (Attendee) is next.

Q48: My name is (Attendee). I'm a registered pharmacist. I work certified in oncology pharmacist. I specialize in hematological malignancies and I'm here for information and I find out I also give talks for the Leukemia Lymphoma Society on agents and I also glean more from the patients than I do from lectures. So, I'm here for information gathering because this is such a rare disease and (inaudible 1:31:26). So, thank you for letting me be here during your journey. Thank you.

Q49: It was no wonder I thought she was a doctor all along when she was asking some of the really pointed questions. She's a drug dealer.

Jean Ridgeway: That's a good one.

Q49: Thank you.

Q50: I'm (Attendee). I just (inaudible) and she'll explain it.

Q51: I'm (Attendee). I was diagnosed two years ago. So far, I just have anemia, but I do get Aranesp injection every three weeks. Other than that I feel great. I don't even... can't even tell

that there's anything wrong, but I want to get information so if they go in a different direction, I want to be prepared and (inaudible 1:32:15) facing or any new treatments that are out there. I want to know about them.

Jean Ridgeway: Welcome back. I met them originally in Columbus. I think they were (inaudible 1:32:25).

Q50: I thought you were (inaudible)

Jean Ridgeway: Go ahead.

Q51: I'm (Attendee) and this time I'm here with my sister, but I have a question. What's the percentage rate of deaths when they do the bone marrow transplant?

Jean Ridgeway: Well, you have to be a little bit more specific with that in order to get an answer. So, I'm not quite sure what your (inaudible 1:32:59) is.

Q51: They said there was a percentage rate of somebody dying. Does it happen very often?

Jean Ridgeway: So her question is what's the percentage death rate. There's so many variables. So, I think the first one you have to consider is what's the age of the person? What's their disease status? What other medical issues do they have going on? Are they diabetic? Do they have congestive heart failure? Whatever. Are you looking at just in the MDS realm?

Q51: Well, she has an... I guess her cancer doctor is a little afraid of the transplant and I went to you in Columbus.

Jean Ridgeway: And he's the head of the transplant (inaudible 1:33:48)

Q51: Well, we're in Springfield. So, she goes to the Cancer Center in Springfield, but at OSU, they after 65 they don't that.

Jean Ridgeway: There is (inaudible 1:33:56) in a country that if you're 55 they don't do it. So, if you're a health consumer which we all are, you got the (inaudible 1:34:03). So and I think probably the best thing you could do for yourself is get a second opinion to hear somebody else's thoughts and ideas because there are transplant centers across the country. We're not the only... we are not the only game in town.

Q51: And I go to the James.

Jean Ridgeway: Which is in Ohio State.

Q52: Ohio State and I talked to Dr. Devine and I'm 65 in October and I think that there are a lot of different things that they look for before they consider to give her a transplant because I would be eligible for a transplant.

Q51: Right, but you're not 65 yet. She's 72.

Q52: Okay. No. But even after 65 they would still transplant me if I'm still in the same health that I am except for this MDS. I don't know what they would do if I was 72.

Jean Ridgeway: Just like Dr. Sekeres said this morning, it's a very individual decision. There's so many variables. It's not... There's just not one answer and do bad things happen when people get transplants? Yeah. Do bad things happen if you drive on the highway? Yeah. So, I mean life is... there's no guarantee. The (inaudible 1:35:26) transplant is a "risky" or a "high risk" procedure and you do have to be medically cleared. So, there are a lot of factors to consider. The number one concern after a transplant is how do people meet their demise basically. Is there a risk of death? The answer is yes. The number one cause of death is relapse of disease. That still remains number one, but infection is right after it and that doesn't change if you're 25 or 65. That's just the data and so if you look at some of the other treatments as well if people can stay in remission with getting a monthly cycle of Dacogen or Lenalidomide you kind of have to weigh your options and I think the other piece of it and those of you who are in care can speak to trusting your oncologist and knowing that they're up to date with all the current information, they know you, you're verbalizing what you want and what you don't want and that really... together you come to a decision. Alright. Next to her is (Attendee), her sister.

Q53: (inaudible 1:36:47) and five months ago... I was diagnosed with this and so the doctor tells me I have one to three years to live and not eligible for a transplant and I'm just here to find out something new.

Jean Ridgeway: So, tell me... I don't know the geography of Ohio, so where is Springfield, Ohio or is it...?

Q53: It's about 40 miles out of Columbus.

Jean Ridgeway: Have you gone for a second opinion?

Q53: No.

Jean Ridgeway: You know, I'm telling you, you have to go for a second opinion. If you have a rare disorder and so in some cases patients will say I'm the only MDS patient at my doctor's office and so that may or may not be a benefit for you and I would strongly urge you to go to a Center of Excellence and Allison Walker is at the James Center at Columbus.

Q52: I've been there.

Q53: Or you could come here... You almost got a second opinion here today.

Jean Ridgeway: Did you meet with Allison Walker?

Q53: I talked to Dr. Walker and she says yeah, you're going to die in one to three years.

Jean Ridgeway: Oh, wow.

Q53: And that's exactly the way she put it. You're going to die.

Jean Ridgeway: Shop around. We're all people and there's some people who are kind of like hard and crunchy on the outside. They're kind of bristly and that's not a personality that you align with you need to find somebody who...

Q53: He told me I was high risk and got plenty on the blasts. So, he says what you do is go day by day.

Jean Ridgeway: Now, when do people... Have you had any transfusions?

Q53: Eleven.

Jean Ridgeway: Eleven. What type of transfusions? Blood or platelets...?

Q53: Blood.

Jean Ridgeway: Oh, blood. We treat patients into their 80s and you're dad is what almost 90 years old and he's getting treatments.

Q52: How long do you get transfusions?

Q53: Sometimes two weeks, sometimes three and I went four, but I was almost bedridden.

Q52: Did they offer you any other treatment options? Not Vidaza?

Q52: She's on all of that.

Q53: (inaudible 1:39:17) every 23 days. I get it for five days.

Jean Ridgeway: So, you are on treatment.

Q52: Vidaza.

Jean Ridgeway: Azacitidine or Vidaza. For people in this room who have been around for a bit, usually what happens and we'll talk about it some is that when you initiate treatment, when you start treatment often I'm not quite sure what brought you to healthcare, like where you really tired or somehow your disease was diagnosed. Usually... People come to be diagnosed with MDS in a couple different ways. Sometimes they get a CBC because they're going to get something done surgically, a knee replacement, a hip replacement. Other people are very ill. They show up in the emergency room, they may have chest pains because they're so anemic. Some people have repetitive infections, they can't be cleared and then they get a CBC. So, I'm not quite sure what road you took to arrive at the diagnosis and to see a hematologist, but if you're getting diagnosed and you've been ill for a bit then your bone marrow probably really just full of blasts. So, you don't have a lot of those other good cells and so what has to happen is that the disease has to be treated and cleared out and it'll take a number of weeks and months. So usually, four to six treatments. So, if it's given five days out of a month, that's what you're looking at four to six months. Usually, the blood counts get worse before they get better and so during this starting time if you were just diagnosed, you said in June...

Q53: March.

Jean Ridgeway: March. So, you've had treatment, April, May, June. Things can get better before they get worse. So...

Q52: Did you have a follow up bone marrow biopsy yet? Is it working for you?

Q53: No.

Q52: Well, she had first...

Jean Ridgeway: Usually if you've had one when you get diagnosed and then after a number of months they'll go ahead and evaluate again and not all drugs work for all people. These drugs are not a home run for everyone, but it's very reasonable to try because you can stay home and although you need blood transfusions you can still go home after a blood transfusion, but then you need to be reevaluated afterwards and see what's happening. So, either one of three things are going to happen. Either it's working, great and you continue or it's kind of working and you're still going to continue or it's not working at all and then they'll change directions and recommend some different therapy, but there are other people in this room who have walked in your shoes and I agree with Dr. Sekeres, don't give up because there's a lot of other things out there and pairing up with someone who might be a little bit more agreeable with your personality might be helpful.

Q53: I lost my husband two months ago and it's still not helping.

Jean Ridgeway: Oh, that's hard.

Q54: (inaudible 1:42:31) versus your high roads, but we heard the same exact thing from the doctor who we first went to and through the forum in Columbus and the one here, we're hearing a lot of other positive things.

Susan Hogan?: I didn't want to interrupt, but you want a second opinion. (Attendee) is our patient (inaudible 1:42:57) the Foundation. We can set up a preferential appointment up for you with another doctor. That's just an option.

Q54: It's shocking to hear what we've heard. That's just the initial shock. Once... they're trying these different therapies and medications, you have to look forward to the fact that it could get better.

Q53: The only thing think that the education I want is (inaudible 1:43:30) and I think... that's something I'm thinking of (inaudible 1:43:39).

Jean Ridgeway: Well hang in there. Hopefully... but I agree, talk to Sue and Tracey. Again, get some names. Get some names and... I would say also when you go to your appointment, make sure you bring somebody with you like your sister or a friend because oftentimes when you're in conversations that are difficult, it's very hard to process information or be able to ask good questions and so get ready for your appointment. You write down the questions and you... I would say also what's the best case scenario, what's the worst case scenario, what are my options and then the person who's with you can help process that information and write it down so you can go home and work through it.

Q55: I'm (Attendee). My husband, (Attendee), we're from (inaudible 1:44:45), Ohio.

Jean Ridgeway: Is his name (Attendee) because he has a name tag...

Q56: All my life I got into medical field, we had to use my first name.

Q55: He can tell you about it.

Q56: I mentioned a little bit. I was diagnosed... Actually, I went into the hospital from the Cleveland area here, went into the hospital and what turned out to be a kidney failure which they thought was a result of other drug reaction with an antibiotic and then the course of that I was transferred over to another hospital and they did a bone marrow test and that's when the MDS was identified and then I was referred to an oncologist and the oncologist specified it as an overlap disease which he said was very rare and I was told that there was no treatment for it. That's the only possibility was blood transfusions and they would treat infection. Of course,

(inaudible 1:45:43) has a son-in-law who's in the pharmaceutical industry and he made contact with a doctor down at MD Anderson in Texas. Went down to Texas and spent two weeks there. The evaluation they came up with a treatment program that they're administrating back here in Cleveland and I don't think I referred to them to a bone marrow specialist (inaudible 1:46:05) who originally they said there's no possibility of a transplant. He said yes, there is and they identified donors and I'm on the Dacogen program. As I said, I'm on the fourth series of that. It seems to be successful. We're going back down to Texas next weekend for the follow up and see what the next phases are.

Q57: We have a very good friend that lives in Southern California (inaudible 1:46:29) with the MD Anderson and he developed leukemia, too. They just put that into remission. He's home now where probably many of the other places that he might have gone would say you're done.

Jean Ridgeway: When you have a rare disorder, it is to your benefit to go someplace that specializes and 20 – 25 years ago people were calling this disorder preleukemia or a disorder of “old age” and the studies I have been in clinical medicine for a long time and it was in the ‘90s that we were doing the studies with Azacitidine or 5-Aza... Vidaza. That's the tradename and a lot of people didn't think very highly of the study and where the drug actually had after the study closed, there was really no rush by pharmaceutical companies to pick up the drug because they felt like it was such a rare disorder that they wouldn't make any money. So, who picked it up? Money drives the world, but I mean it's interesting to see from that drug got approval in 2004 from the FDA and then how many people are on it, but before that there... you would be the rare bird at your doctor's office that said, oh, there's really nothing we could do for you. There's no options to... So, I mean, a lot has happened in the past 25 years for people who have these bone marrow diseases. So, it's interesting, but again it may not be (inaudible 1:48:15) another proof in point that you just need to seek out some expert's opinion and the Foundation was formed by a patient in conjunction with a hematopathologist, a pathologist that looked at blood slides to really become and advocacy organization for people who have this rare disorder. So, interesting.

Q58: My name is (Attendee) and I'm here supporting my wife, but (inaudible 1:48:41) things that can happen. When my dad was 80 years old, he was diagnosed with lung cancer and they gave him three months to live. This was in December and I said, “Dad, what do you want to do? Do you...” “I want to go home this week and die in the house I was born in and that's what I would like to do.” I said, “Okay. We'll get tickets and we'll fly over.” In December, he said, “I'm not going to Sweden in December. It's cold.” I said, “When are you going?” “When the weather gets good,” he says. He was still alive and I brought him home to Sweden and I left my mom and dad there and they were happy and we'd talk on the phone every once in a while and then he calls me up in October 1, I think it was... The first week in October and he says, “(Attendee),” he says, “It's really getting cold here. It's starting to snow.” He says, “I'm coming back.” So, he did and he lived to be 86. So, you can't give up hope. You got to keep (inaudible 1:49:46) and you got to just be positive that something's going to happen. Maybe God decides he doesn't want you now.

Jean Ridgeway: Right. Exactly. Very true.

Q59: I think doctors like to put the whole in. I mean, the worst scenario rather than the best scenario in a lot of ways, but I was diagnosed with MDS. I was going for back surgery down at the Cleveland Clinic... we're from Florida and they said, "(Attendee), you've anemia," which I knew I had, but they never saw why and so when he said, "Well, I think you need rechecked out by the oncologist," I went there. That was in March of 2013 and they said you've got... they did the biopsy and everything and I have... they actually said I was a high risk because I had so many mutated chromosomes, 19 out of the 20, and I had RARS, refractory anemia with ring sideroblasts. It is not really progressed that much. My hemoglobin at that time was 10.2 and she said the only thing... start on shots. I think the Aranesp (inaudible 1:51:02) my hemoglobin you can start, but I didn't start till over a year later. They started the shots September of last year, September of 2014 and I get Aranesp and it helped a little even though it's most... I think it's only 20 percent of people that are helped by Aranesp and I guess I was one that bases at about point. Most of the time my hemoglobin was 9.6 on last Wednesday.

Jean Ridgeway: People feel better even though the numbers show one value, people tend to (inaudible 1:51:34) say, "I feel better."

Q59: I don't know if it's just a psychological thing because I take a lot of naps during the day, but I try to stay active. I exercise as much as I can. I walk. I've gotten a little thing which I love (inaudible 1:51:51) so it gives me something... somebody to compete with. I try to eat well which is difficult because my husband doesn't eat well and I'm trying to do a lot less chemicals. I mean, so many of our shampoos, our soaps, everything has these chemicals which in other countries they banned and to allow the United States to use something like sodium laurel sulfate is in every shampoo and soap.

Jean Ridgeway: Even the drug dealer can have (inaudible 1:52:29).

Q59: And even chloride. I mean, I said I need some tin foil to brush my teeth.

Jean Ridgeway: So, what brings you here today?

Q59: Here? To get more information, to find out more. I had my oncologist said definitely don't do a stem cell transplant. I'm 74 now and yet then I went to a Shands in Gainesville, Florida and they have a great bone marrow center there and since my other health... I don't have heart problems, diabetes or anything like that and he said, "Oh, yeah. You're definitely a candidate for a stem cell transplant," and so I thought that briefly and (inaudible 1:53:10) pluses and minuses and being my age and everything and I had ironically I have three friends that have forms of MDS although the one might be acute myeloid leukemia and has done cell transplant six years ago and... but she's in her 50s. Another friend had one at 70 and he's dead now. He had it last

year in Chicago and then the third one is I had blood transfusions for three and a half years and gets them once a week now, but he's alive.

Q60: Yes, so I'm living and not a bad life.

Jean Ridgeway: (inaudible 1:53:48) I mean, the toxicities with transplant are very real. It's a very complicated therapy. I mean, (inaudible 1:53:56) chemotherapy and immunosuppression, but there are some other issues that get pulled into that and thinking about quality of life and getting transfusions. Again, it's not an easy decision. Alright. (Attendee) is next.

Q61: I'm (Attendee). I'm a diabetic. So, I get my bloodwork done every three months and the doctors starting saying you're anemic. I want you to get more iron. You're anemic. Okay. Finally, my blood hemoglobin went down to 10.7 maybe like that and I mean I couldn't even bend over to pet my dog at that point and it was just kind of new. So, he sent me to Mercy Cancer Center in the area and they did a bone marrow insert. (Inaudible 1:55:00). How much pain medicine they give you on the outside, but in the inside is (inaudible 1:55:07). Anyway, so I finally got diagnosed with MDS in 2008 and since 2008, I kind of jumped up from 10.7 to 9.6, the lowest, and when you get that low and... on me I was telling (Attendee) here that I felt like I was dead and I told my doctor I feel like I am dying because...

Jean Ridgeway: With the low hemoglobin.

Q61: Oh, God. Yeah. So anyway... and then the doggone insurance lowered my blood hemoglobin count to 9.9. If I went down to 9.9, I can't get the Aranesp shot.

Jean Ridgeway: You cannot?

Q61: I can. If it's 9.9 or less. Well, I've been 9.9 and less the last several months. The insurance doesn't want to pay for it, but I think the Cancer Center is absorbing most of the cost. It's been up and down.

Jean Ridgeway: So, you've gotten Aranesp.

Q61: Yeah. I got the Aranesp shot. I mean, I just had one so... but I come to these because I want to see if there's anything else something other new I can learn when there's a few things, yes, I'm definitely going to ask my doctor about where do I fall on the blast zone and I definitely want to ask him to do another bone marrow.

Jean Ridgeway: You are?

Q61: I am. (inaudible 1:56:49) 2008.

Jean Ridgeway: Two thousand eight? You're due.

Q61: I just may be... I mean some of you are a lot worse and I thank God that you're still here and I thank God that I'm still here.

Q62: And I think you're going to find with the bone marrow biopsy maybe it's changed. I've had four in the last year. I never had any pain and (inaudible 1:57:27).

Q61: Terrible pain.

Jean Ridgeway: Take a couple Tylenol before you go.

Q61: I'm going to take something stronger.

Jean Ridgeway: Or you can take something stronger, but it's true that a lot of discomfort is before you get a bone marrow is not healthy. If you're in remission and things are better it's as not as discomfort, but... Everyone is different and there has been a big push lately even with the American Society of Hematology and it's called just stewardship with transfusions and we have a threshold that we set and our patients are seven and a half or seven grams per deciliter of blasts, but we don't transfuse people until they are really low unless folks are very symptomatic, but... and that's the big push in hematology is just to lower that threshold.

Q61: What's the purpose of that? I heard it was quality of life.

Jean Ridgeway: So, it's interesting. You look at like the medical perspective. Transfusions first of all are not benign. There's always a chance of infection. There's also a change of iron overload.

Q61: (inaudible 1:58:49) that we have them. Is that so?

Jean Ridgeway: You never excrete the iron. So, you got 200 milligrams of non-excretable iron per infusion. So and that deposits itself in organs and can cause some (inaudible 1:59:02) organ damage.

Q61: And after having them for a while though or can that happen immediately?

Jean Ridgeway: Well, you immediately begin to absorb all that iron, but you're right. We check something called a ferritin level and when the ferritin level begins to rise over... some people use 1,000 to begin to treat that or not, but so it's really the push from the medical community.

Q61: To lower the number?

Jean Ridgeway: (Agreement) to lower the number and honestly some people they begin to... the do acclimate.

Q61: Yeah, my dad is around 8.9 and he's almost 90 and he's doing really very well. Maybe it's a coexisting diabetes.

Q60: It could be that or there's other disease I have but...

Jean Ridgeway: And that makes it much more complicated, not very simplistic. So, things get... you have to be balanced. In some areas of the country, I live in a large urban area and our blood availability is good, but you go to some more rural parts in the country, it's not so. When there are natural catastrophes like the Katrina, the blood banks in that whole area were down for a long time. It's a scarce resource. I always tell people families are like what can I do to help and I'm like well, why don't you donate. Do I donate blood? Do I donate platelets because it's a nonrenewable resource and it's a total volunteer pool. So, that's how it's (inaudible 2:00:29).

Q62: I have a question. My dad has not had a transfusion yet and he's so far doing pretty good as I said. He's a little bit nervous about the idea of getting one. Old, (inaudible 2:00:44) notions about transfusions are danger of tainted blood. Is it better to have your family donate the blood for someone like (inaudible 2:00:54)?

Jean Ridgeway: If you're a match, that's fine. I'd say go ahead and donate.

Q62: He's O positive. Do you have to have an O positive to donate or is he a universal receiver and donor?

Jean Ridgeway: So, the O is universal donor, AB is the universal recipient, but when blood banks have blood they test 269 antigens on the red cell. So, there's a lot of variability within that as well as a myriad of infectious disease markers and sometimes you don't pass the muster to be a donor either. So, you can try to donate. I think that would be fine and ask about the... It's called direct donation. So, they'll have that dad's type of (inaudible 2:01:34) but if you donate the red cells, they're viable for a number of weeks. Sometimes they get frozen. You can ask, but it's called direct donation and then say that you donate, you're a match for your dad, they don't use it they'll ask you to sign a consent can they release it when it comes near the expiration date, so that someone else can use it.

Q62: Thank you for that.

Jean Ridgeway: Alright. Who is next? The gal with the broken wing.

Q63: I'm (Attendee). I'm here to support her because I know how it is to have a rare disorder and (inaudible 2:02:08) mutation.

Jean Ridgeway: What happened to your arm?

Q63: I had a patient fall on me at work. I'm a transporter. I think I tore my rotator cuff.

Q64: That was almost a year ago and we were (inaudible 2:02:30) MRI. The insurance company (inaudible)

Jean Ridgeway: (Attendee)

Q65: I'm (Attendee) from Columbus here with my husband, (Attendee).

Q66: And I am (Attendee). I was in 2006 my personal physician noticed my blood lines were starting to fall and watched it with the yearly physical for a few years and then finally said you need to see a hematologist because it kept falling every year. So, December of 2011, I was diagnosed with MDS. This is in Columbus. I decided to come up here to Cleveland Clinic for a second opinion to see one of the doctors here. I had a bone marrow biopsy up here. He concurred in my hematologist in Columbus the diagnosis that I had MDS also concurred that I also trying Vidaza. So, I started on Vidaza in January 2012 (inaudible 2:03:34) Vidaza for a little over three and a half years which as I understand is kind of a long time for someone to continue to be effective. I've never felt throughout this whole process any symptoms. I've never had fatigue. I've never had bruising. My hematologist had nothing to say to me. If you didn't come to see you wouldn't know you were sick. He decided after the Vidaza had been working for two years which was a pretty long time that I ought to look at the possibility of a transplant and so I went to the James and talked to a transplant doctor there. Had another biopsy. They found a perfect match for me and I was eligible for a transplant, but the doctor there said that this Vidaza working so long, it's unusual, but who knows. This could go on for many years. It could stop next month or it could go on for years and as long as that's working, I don't think we should disturb it. So, I will be eventually pressing the limits. I'm 70. So, I think 75 as I understand it at the James they won't do one after 75, but things are working well and continue to be active. Play tennis several times a week and...

Q67: Well, (Attendee), you look good.

Q68: When I went to Shands, there was a patient just leaving that was 79 or 80 and I don't know if it was... he had a transplant, I'm not sure what it was for.

Jean Ridgeway: So, multiple myeloma is another malignancy but even with myeloma, we've done 77 to 78 year olds. (Inaudible 2:05:19) again, Medicare is the gatekeeper with insurance approval. I don't know. It's a line that you need to move forward. We are a country approach (inaudible 2:05:33) and respond appropriately. So, I'm not sure. I've never seen someone over the age of (inaudible 2:05:41). I mean, it's really hard. It is really hard and so... anyway...

Let's see what kind of... So, a lot of this information that I have is a repeat of what you heard this morning as well. These are just the people that I have the opportunity to work with and what's really interesting is that in other parts of the world, MDS don't occur. Countries that get locked into the vacuum and think that we live in a silo and they (inaudible) that country. It happens globally. It's a global disorder, but treatments can vary by where you live in the world. So, that's just the way it is. Anyway, so these are just like kind of questions and you've got your nice... both of those are the same. So, I think one of the... the best things that you all can do and really... you become the poster children for being advocates for yourself even by attending. So, you take ownership of your healthcare and you want to know more about it. I think a well-armed patient is somebody who at least makes the effort to go out there and begin to understand things and it's very complicated. Even in my doctoral program, we talk about malignant hematology, but not a lot because it's still a rare disorder. There are not a whole lot of people who are as well informed as you and if you go to events, when you go to a doctor, you may be more informed that they are. Community oncologists see a lot of breast cancer, a prostate cancer, a colon cancer, breast cancer, but they not see a lot of blood cancer and so the culture and the amount of information that's out there are changes at such a rapid pace, it's difficult to keep up on.

So really, we'll go through some of these things, but I think... pick up the book and if you haven't visited the website, make a spot check and visit the website. What you have in your hand is available via the Internet in this really nice little format where it turns the pages for you and it also has interactive videos on it which are pretty neat and so a lot of thought and time went into developing it. So, we'll talk about that a little bit.

So, we talked about this earlier. People went around the room because we asked you what MDS. Some people gave some very sophisticated answers. It's a bone marrow failure disorder and that I think you realize that it's really a whole group of disorders. There's not just one type. (Attendee) sitting next to (Attendee) has a similar disorder, but not an identical disorder and remember that as you go around and talk with people even in your clinic that it's not an apples to apples comparison and be careful because it's easy to compare yourself with someone else and there's so many unique things about your health and your disease that need to be taken into consideration. So, what we know about MDS, too, M stands for myeloid and so in the world of blood development there's a mother cell called the stem cell. So, we've talked a lot about stem cell transplant. So in the blood itself, this stem cell when it begins to make a decision to grow up the first decision point is do I become a myeloid cell or a lymphoid cell? So, the myeloid cells are the red cells, the white cells and the platelets and so the M in myelodysplastic syndrome means that myeloid of families. Now, there's another family called the lymphoid side and that's people who have... if you have friends or if you ever heard of multiple myeloma. That's a lymphoid malignancy as well as acute lymphoblastic leukemia, chronic lymphocytic leukemia. Those are lymphoid disorders, but this a myeloid disorder and if you think about going backwards, if you were to go to a factory. If you go to the factory and watch the product come off the line, you would want to know like why is this product defective you have to go back to

the origin source. So, you go back to the stem cell. So, we know somehow the DNA in that stem cell has been altered and the development of the cells is no longer normal and that can show itself in a lot of different ways. Some people have low red cells. Some people have low white cells. Some people have a lot of blasts. Some people don't have that many blasts. So, really a very mixed picture of what it can do and again, we see it in a lots of different places, lots of different environments and for each of us and for each of you it really holds a different meaning because it is so very different.

So, the D in Myelodysplastic Syndrome says dysplastic and what that means it's an abnormal shape. So, a number of people in this room have been in a car before, correct, and so the wheels on a car are round. So, if you changed the shape of the wheel on a car, you made it kind of oval or square, your car would still go, correct, but the ride would be a little bumpy because the function of the car is going to be affected by the shape of the wheel and that's what happens in this disorder, too. The function of the cells is disrupted when they're abnormally shaped and when you step even further back from that that abnormal looking cell is being driven by things unseen, the molecular pieces that are growing off the cytogenetics of the DNA (inaudible 2:11:42) and so that's what the D stands for is dysplastic and S is for syndrome and then we have something called cytopenia. So, that's the generic term for when blood counts are low, but if your red count is low we call it anemia. If your white count is low we call neutropenia and if the platelets are low we call it (inaudible 2:12:06) cytopenia. So, those are all big fancy words. If you play Scrabble or if you're a Scrabble fan, you could win, but spelling them right and what about the risk of developing leukemia. They're just like Dr. Sekeres said. We've drawn this line in the sand that says 20 percent or greater is leukemia and this is really the truth that if we... say we do a bone marrow on (Attendee) and we're looking at a clinical trial for her and think she's going to be a great candidate for this MDS trial and the pathologist looks at the slide. If it's not very equivocal like if she has 90 percent blasts that's an easy call. If she has 19 to 20 percent, he sees is 19 percent because I need her on this MDS trial. So, there's a bit of wiggle room. It's not an exact science. Literally when they look at these slides under the microscope they're counting, but there estimating. They don't go one, two... that's not how it's done. So, there's a bit of estimation as well, but it is true for some MDSs but not all. They can progress to acute leukemia, but what the data tells us now that we've been following patients with MDS for a long time is that the majority of patients don't progress to AML. They succumb to other illnesses in their life. It can be a heart attack. At the age of 90, your dad's kind of like... he's lived a long time. Anything can happen. The one thing that's very true about all of us is we're mortal beings. It's just the fact of life. So, you can't really say what's going to happen.

So, this a better picture. Since I don't have to draw you can tell that I also failed art when I was in school. I draw bad stick people, but this is I think a nice picture of what a normal bone marrow is. So, this is just a fancy... and so here's your stem cell and here's these stem cells and these are the cells that when we look at your CBC we see neutrophils. These are some other fancy white cells, platelets and red ones and then there's the lymphoid cells as well and that's how it should happen. It happens all the time all through our lives. It happens consistently and there's this nice

balance in life called hemostasis that when cells die that they're replaced. So, there's usually an absolute balance and the other really neat thing about bodies is that when cells grow old they die, but in MDS oftentimes what can happen is that there can be an overproduction of some types of cells and under production of others. So, that's when things begin to get out of balance.

So, what we see in MDS is that the bone marrow environment becomes disrupted and instead of seeing something nice and healthy what you begin to see is something very abnormal and then you have an overproduction of the immature cells and we call the immature cells blast cells. So, as the stem cell grows up. So, there are different triggers along the way that cause a (inaudible 2:15:26) potent stem cell to become a functional red cell – hormones, cytokines, lots of fancy shmancy stuff in our body. So when that's disrupted or altered and there's a genetic problem they stop in development and so they get arrested and they stop in the blast phase and unlike normal cells that die when their useful life is over they don't. So, they continue to replicate and so that's why you get more of them when you would want to get less of them and when you have too many of the baby cells in there what it's going to do is it crowds out the good ones and so I'm not a gardener. I really don't have a green thumb but one thing I notice that if I had a garden and I went away on vacation in the Midwest and I don't leave anyone to tend my garden when I come back the weeds do better than the plants. They're exposed to the same nutrients, the same weather, but for some reason those weeds do better. So, they tend to be more opportunistic and that's how these bad cells are in your bone marrow. They will outperform the good cells. That's just their biology and so they become the hindrance to normal blood development and sometimes what can happen... what often happens is that although there's many of them they do contribute to how your bone marrow produces blood cells. So that at the beginning of treatment with Vidaza or Dacogen we see the counts getting worse before they get better and I have another slide for that, but that's because now I've gone through and I've pulled all the weeds out and what's left are my straggly tomato plants that look just miserable and will they come back? Yes, but it's going to take a little time. So, that's what happens when you start treatment.

How is it diagnosed? So, we heard that (Attendee) was having a sharp primary care doctor who said you have anemia. (Attendee) was going to go for back surgery. Ms. (Attendee) over here wasn't feeling well. I don't know how your dad got diagnosed, but...

Q69: He was feeling a little fatigued and weak and just had routine bloodwork done.

Jean Ridgeway: See. So, there's lots of different (inaudible 2:17:39), but one of the things that needs to be done... I mean, there's a whole workup that needs to be done because sometimes things can masquerade like MDS and you want to make sure that you don't have one of those. So, some things can be kind of fixable. People who have Epstein Barr virus which is mild. That can cause anemia. I've seen that in younger people not so much in older ones, but there's a certain amount of information that needs to be gathered and for the people who are in this room who have MDS we know you do need a bone marrow biopsy and an aspiration.

Q70: There seems to be a common thread here that people find out about it by accident. Are there any estimates of how many people might have MDS that have never been diagnosed? Have there been any correlations that involve (inaudible 2:18:28)?

Jean Ridgeway: What they do is they do projections and so anytime you see data that looks at from the American Cancer Society like X amount of cases of this disease are going to be diagnosed. It's really looking at the data from the previous years and doing some epidemiological (inaudible 2:18:47) numbers. One of the things I will tell you that a lot of data gets generated from insurance databases as things get coded. So, they look at anemia, but there's no real way to say who's living with undiagnosed anemia that may truly be MDS.

Q70: There must be a lot.

Jean Ridgeway: There could be.

Q71: That is a very good point. There are a lot undiagnosed.

Jean Ridgeway: There probably are quite a few. One of the studies that we do is we work with our primary care office providers as well as our geriatric providers in that if someone has an unexplained anemia, some anemia is explainable – iron deficiency. You have to do the right tests to figure that out and then some people have B12 or B6 anemia. So, I know vitamin deficiency, but an unexplained anemia means that those things are not true, why does this person have anemia and we're trying to enroll people in a study where we look at their peripheral blood and we ask them to do a bone marrow biopsy to see if we run these tests are they falling on a continuing and (inaudible 2:19:56) early diagnosis. So, some people are exploring it. A lot of people aren't very excited to do that. A lot of our patients are really old. They're like 85 or they're close to 90 and this person I did a procedure on he was 95 years old. He was quite a champ. He was quite a champ. So, he did that.

Anyway. So, what needs to be done? So when we do the bone marrow biopsy what are we doing? Well, some slides go to the hematopathologist. These are people whose job it is to look at the slides under the microscope and they know normal from abnormal. That's what they do. They look at all the blood kind of things and what are they looking for? They're looking for what is there? How much of it is there? So, are there normal cells that are abnormal cells that are dysplastic? Are they normal? How many blasts are there and, again, all of us have blasts because as the stem cell grows up, the blast formation is normal and you can have up to about five percent in your bone marrow and that's okay, but if you tip over into six percent, we start looking at things that aren't okay because you shouldn't have that many. Then we do something called cytogenetics. So, cytogenetics is looking at your DNA and so we look at it from the bone marrow because we're interested in the DNA of those blood cells. So, why do people do cheek swabs when they want to find out who's the baby's daddy? You know how they have all these

crazy shows and people who call and strangle each other on the stage. So, how they do that is just from a buckle swab that buckles right at the inside of your cheek and that's your constitutional DNA and so we can go ahead and grow that out, but that's not going to show us if your bone marrow cells... if your blood cells have an altered DNA. So, that's why they do that. So, we look at that and you can have anything from normal. So, 46XX says I'm a little girl. I have 46 chromosomes, I have 23 pairs and XX says I am a little girl. Forty-six XY says you're a little boy. If you have 5Q- that means on the fifth chromosome... Chromosomes are very interesting. They only have arms. They don't have any legs. So if you ever seen a picture of it, it looks like a short U on top and an inverted U on the bottom. So, this is the upper arm and this is the lower arms. So, the upper arms are called P or petite. That's how you remember that and the ones on the bottom are called Q. So, when you look at somebody with a 5Q- syndrome that means on the fifth chromosome a Q arm there's a piece missing and not the whole thing usually. As you say it's an (inaudible 2:22:35) but that's what that means. Some people can have something trisomy 8 and you say it's an additional eighth chromosome. So, if you want to be silly you can go on Google images and you can look it up and there's lots of information out there on chromosomes and there's some good information in the book as well as that little book about 100 questions they talk about that as well.

Q72: Can your chromosomes change during this process like if everything is fine and dandy today six months from now are your chromosomes the same?

Jean Ridgeway: Yes. Can your chromosomes change? Yes and it's called evolution.

Q72: Okay and then from that like if none of your genes are mutated but when the chromosomes change can your genes then mutate? Is it (inaudible 2:23:16)?

Jean Ridgeway: So, genes are in the chromosome. So you could have 5Q- and you could treat it with Lenalidomide usually and then they do the bone marrow and there's no evidence of 5Q- or you can have a bone marrow transplant and your sister is your donor and you're a male, you'll end up with 46XX chromosomes. Your blood chromosomes will be female. Your constitutional will remain male, but in MDS things can change. Things can revert to normal or sometimes things can progress and have further changes.

Q72: Do the blasts ever go down?

Jean Ridgeway: Do these blasts every go down? (Agreement sound) If you do treatment, blasts will go down. These are, in general, are not diseases that go away.

Other tests that they do. They look at iron. Why do they want to look iron? Well, you have to have iron in your body to make red blood cells and the best test of iron is in the bone marrow and then they do other things – B12, folate, they do EPO levels. Why? Because they want to see if you're a candidate to get Epogen because if your EPO level is low then we know giving you

Epogen is going to help you. You can think about Epogen like a glass of water. If your glass of water is full and you pour more water into it it's just going to spill over. Can you really benefit at anything? No, but if your glass is half full and you pour some more water in it, it can help you. So even Epogen can help you if you're low on Epogen. How about TSH? That's a thyroid stimulating hormone. If your thyroid is a little bit sluggish which can happen with age and happens also if you have other illnesses that also can attribute to anemia. Testosterone is another thing that needs to be checked for men and then you just have to look at kidney and renal function. So, all those things were done. It's a workup for your MDS one other way and they looked at not only establishing where you fell on the WHO, but then they went to the IPSS score.

So, this is just another look at the classification systems. I'll tell you that in the early '70s the first classification system really came out. It was called FAB for French American and British and that's because it was collaborative effort between the French American and British hematopathologists to speak the same language because until the early '70s people didn't have a common language to speak in this disease. So, they got together and, again, that's five major subtypes and RA or refractory anemia is the backbone of it. So, RARS is refractory anemia with ring sideroblasts, excess blasts and then unique to the FAB is something called CMM out or CMMO (inaudible 2:26:06) monocytic leukemia. That's more of a myeloproliferative disorder. So, that's the MP kind of crossover, but and then the World Health Organization came out and this is another consortium and it's an international effort and they said, you know, that FAB is great. What it doesn't talk about what do things look like under the microscope, but we have to know more about cytogenetics and molecular markers. So, somehow we need to begin to fit those pieces in and so they began to do that in the early 2000s and so you see more categories. So, deletion 5Q is first really described then. If you had deletion 5Q back in the '70s, you would have just fallen probably into refractory anemia without the true origin of what the abnormality known. The other thing they began to change is the definition of acute leukemia. Again, they used to say in the FAB it was 30 percent and then you would be leukemia. Now in the WHO, they say 20 percent. So, a bit of a change there and then in 2008, they revised it and, again, added more data into the knowledge base because some people have something called refractory cytopenia with multilineage dysplasia. That's RCMD. MDSU means MDS unclassifiable. You may fall into that, (Attendee), and they also began to take more of the proliferative disorders out and put them into their own separate little circle over here called MPDs or the myeloproliferative disorders and this just lists that this column is from dysplasia. So, how many lines look funny. Don't really have normal shapes in them. They look at the number of blasts there. So, different classification systems and sometimes if you get a hold of your medical records which belong to you or belong to your dad you could read the report. So, there's usually when the bone marrow biopsy report comes out there's usually a paragraph that gives you the summation. It's kind of like cheating when you read a book and you like flip to the last page and just read the end. So, you want to read that last paragraph first because it's going to give you the summation and that goes on to talk about lots of other things, but that's where you want to look.

So, you guys talked a little bit about this, the IPSS scoring system and now the IPSS-R. It takes three pieces and puts it in together for some type of scoring system and this is really valuable. So, you were asking (Attendee) questions about how... like why does your doctor say like how long am I going to live. Why do they give you that type of prognoses? I would imagine they probably took the data, the numbers from your bone marrow and kind of put it in, but again when physicians quote patients numbers they're just numbers and you're talking about the middle. In medicine they talk about the median survival. That's kind of like smack dab average, but there are people on either side of that. There're people on way on the outside of all of that, but it's where it's coming from and it really becomes the primary decision-making as far as what are we going to do for treatment.

Where's my guy? Come up here. So, we're going to try to experiment. You ready? So, we're going to go on the website and would anybody be willing to volunteer to give us their numbers from their bone marrow and we'll plug it in? Want to see how it works?

Q73: I have them.

Jean Ridgeway: Pull them out.

Q73: Which ones do you want?

Jean Ridgeway: First I need your... so this is... if you got your bone marrow report.

Q73: I do.

?: So, the calculator is available (inaudible 2:30:10).

Jean Ridgeway: So, this is on the website and if you have the book or you can just do IPSS-R in Google, you get pushed that way. She's going to pull her numbers up.

Q73: Okay. This is from my last marrow biopsy.

Jean Ridgeway: So, just a thought when people get an IPSS score, it's not meant to be tracked through the illness. Usually, IPSS score is done at diagnosis. Will it change? Yes, because you know your numbers probably change, but when you go to the hematologist this is honestly we do this in the work room. So if you came to see us, we have all your records, we look through everything, we talk about what's your IPSS score and then discuss it with you. You ready? How about your hemoglobin?

Q73: Oh, then let's look at this one.

Jean Ridgeway: It probably says it right on the pathology report.

Q73: I have a couple reports here.

Jean Ridgeway: Oh, dear.

Q73: This is my most recent surgical (inaudible 2:31:21).

Jean Ridgeway: Do you have the one that you were diagnosed with?

Q73: Oh, gosh. You know what...?

Jean Ridgeway: We're going to go after this one. Alright. So, her hemoglobin is 12.6, absolute neutrophil count... It's 1,000. Platelets are 158. Bone marrow blasts 10 percent. Cytogenetics, I don't know if it's on here.

Q73: Where would it be?

Jean Ridgeway: It may be on a report that says cytogenetics. That's the CBC. Keep going.

Q73: (inaudible 2:32:40) that is where the bone marrow blast is. It was (inaudible)

Jean Ridgeway: Sorry. Bear with us. We could make something up, but we didn't want to make your heart drop to the bottom of your stomach. Would you be like complex cytogenetics? Normal. Just 46XX. We're going to say you have... very good.

Q73: This is what my doctor (inaudible 2:33:24)

Jean Ridgeway: So, put very good. So I would go ahead and hit the magic score. So, we're going to do the calculator button.

Q74: Absolute neutrophil count. I'm sure I'm saying that...

Q73: (inaudible 2:33:37)

Jean Ridgeway: Put down .8. So according to these numbers, which may or may not be correct...

Q73: They don't do me very good. (Inaudible 2:34:09)

Jean Ridgeway: Well we gave you very good. So, they say the IPSS score, the revised, is two and the category that you fall into is low risk. So now, we're going to do another one. We're going to make this one up.

Q75: Can I do my dad's?

Jean Ridgeway: You can do your dads. Okay. So, we'll start over again.

Q76: But hers said good instead of very good.

Jean Ridgeway: (inaudible 2:34:31) changes it to a three. You want do it again?

Q75: it was 10.4.

Jean Ridgeway: So, 10.4 for the hemoglobin. Do you happen to know what his neutrophil count was?

Q75: The neutrophil was 1.5.

Jean Ridgeway: Do you know what his platelets were?

Q75: Platelets were...

Jean Ridgeway: Were they normal?

Q75: They were normal.

Jean Ridgeway: So, put down 200. Bone marrow blasts?

Q75: Thirteen.

Jean Ridgeway: Thirteen and do you know what his cytogenetics was?

Q75: Intermediate.

Jean Ridgeway: Okay. IPSS score 5 for high and the category would be high.

Q75: I think the platelets were higher than that. Would that make it better? I said his number was 4.5, but that's pretty close.

Jean Ridgeway: Well, we're pretending here because we really don't have the data.

Q75: I can't remember what the numbers were.

Jean Ridgeway: But that's how it works and so we can do... Let's do another one. We'll do a hemoglobin of nine.

Q77: It was higher than the doctor would more be thinking about the Vidaza (inaudible 2:35:40).

Jean Ridgeway: And treating that.

Q77: Along with the blood transfusion.

Jean Ridgeway: Maybe if the person needs it.

Q76: Hemoglobin was (inaudible)

Jean Ridgeway: And then we'll do neutrophil count we'll do 2.5 and then we'll do platelets 200 and we'll do bone marrow blasts four and we'll say karyotype good for like a 5Q- and then we'll do the calculate and so the IPSS-R score is three and that is below... That's kind of somebody with who has 5Q- oftentimes has anemia only, a low percentage of blasts, so but that's how the IPSS-R score.

Q78: I read an article that even with people have low risk if they have very low platelets that's associated with a poor prognosis. Have you seen that?

Jean Ridgeway: No.

Q79: So on the report, on the bone marrow blasts I can't seem to find that on any of my reports.

Jean Ridgeway: Oh, come here. I'll show you. So, let's make sure we're looking at the right thing. This is CBC. So you won't find it on here. You have to look for something that says like surgical pathology. These are your cytogenetics.

Q79: Right.

Jean Ridgeway: And that's not going to say it either. Keep looking.

Q79: It'll just say bone marrow blasts?

Jean Ridgeway: No. It'll say surgical pathology and then you could find the number of blasts on that. So anyway, that's just how it works. If you were interested or you know how that thinks. Don't go far.

?: Should I close the window or keep it open?

Jean Ridgeway: Close the window.

?: Alright. I don't usually get to participate.

Jean Ridgeway: Anyway and so there's actually an app on the phone, which I'm nerdy enough to have because we see patients all the time. So, we happen to do that so we use it, but that... and it's not that someone just kind of... it's all data driven. There's all type of algorithms that are built into this to come up with a calculation. So, we heard this before. Sixty-two was too low. Average age 72. So, we were off a little bit. We do say that it's a malignancy and that transplant is the only cure, but with it comes a lot of risk and not necessarily a longer life and the leading cause of demise is really the disease itself and this risk stratified treatment strategy that's that whole IPSS. If you're a low risk the recommendation is something; moderate so that's what a risk stratified (inaudible 2:38:25) is all about.

So, when do people decide to do treatment? So, it's usually triggered either by... It's a couple things. It could be transfusions like (Attendee) in the back was having transfusion when she got diagnosed and so perhaps the transfusions... some people are happily along just a wait and watch kind of thing and they're fine with that and we see them on a regular or an irregular basis, but then we've got folks who have a lot of blasts, etc. and then again we want to make an individualized treatment decision. So, your dad is fortunate that at 89 he's pretty robust. That's not necessarily true for all 89 year olds, but it can be for him and then you want to look at all these and comorbidities, how many other medical illnesses does the person have. Are they somebody who goes to water aerobics and drives taxis, overly active or are they somebody who really spends the majority of time in bed and that's going to drive what's really possible for the person as well as their caregiver. So, it's nice to see that the majority of people here today are here with somebody, but because it takes a lot of effort to live with a chronic illness and back and forth to the clinic and appointments, etc. So, and then you want to look at lifestyle. What are people really looking for and so we talked about this before. What are some other treatment options? Certainly transfusions are the backbone of treatment for MDS and in Europe they call transfusions active care. They don't call it supportive care. In fact, it's actually considered a treatment because it is a therapy.

Q80: Why does anemia and MDS go... be part of it? Is it something going on because MDS you think of anemia?

Jean Ridgeway: So, about 85 people who have MDS do have anemia and that has everything to do with the development of the myeloid cells and because the red cell precursor is a myeloid cell.

Q80: So, something in the myeloid environment or some of those cytokines like you said are (inaudible 2:40:41) or something...

Jean Ridgeway: Maybe more people have lower neutrophils or platelets, but so many times when people are anemic it brings them to healthcare with chest pain, shortness of breath, fatigue. You can live with a chronically low white count and unless you're getting repetitive infections, you're

not knowing it. Nobody's getting their CBC drawn at Walmart yet. So, you're really aren't aware of it. So, I think it's a combination of those two things.

Q80: Somethings not telling the stem cell to take the red cell line rather than the...

Jean Ridgeway: Well, it's still along the same lineage.

Q80: But that seems more effective taking more...

Jean Ridgeway: We see it a lot more. Absolutely. You certainly do. I don't know the exact answer.

Q80: I don't either. That's why I'm saying it seems like it's a common thread.

Jean Ridgeway: Yeah. That is up to 85 percent of people have a component of anemia. So and we talked about all these different treatments and then investigational agents and I think it's great that he showed you a bunch of slides that had some drug development and different things that are out there. So, this is just a grid of some other therapies that are under investigation and, again, the sky is the limit as far as what's available. If you like the Internet, you can go to nci.gov for government and then you put in the acronym MDS and you can see what trials are available, but you may have to travel. You may have to go to Cleveland. You may have to go to Ohio State. You may have to go to MD Anderson because not all studies are available at all institutions. So, you need to kind of scrutinize it and the other thing to look at if you go to that website, they'll describe the clinical trial and they'll tell you about something called eligibility criteria. So, you can think about that as the key that unlocks the door. My key doesn't open your house and your key doesn't open my house door. So, they're looking for a select group of patients. So, a study may be designed for people who have already had Vidaza and perhaps now they don't respond to it. So, they want to look at that group of patients for this... for drug (inaudible 2:42:59). Some studies are designed to low risk people or people who need transfusions, people who don't. So, there's a lot of different options out there. So, this is just some of them and usually if you enter into a clinical trial there are some costs that are covered, but the majority of the costs that they're considered standard of care are not. If it's a drug they're supplying, you're going to get the drug for free, but if it's an intravenous drug you may still have to pay for the administration route or the saline like our drug dealer over there. She knows that (inaudible 2:43:33) cost money and so somebody has to pay for it. So, there's some costs that get shared and some that they own. There are some studies that they do something like really heavy and they want to do something very investigational. Some of those procedures might be covered like there may be additional bone marrow biopsies to see and sometimes they're covered as well.

So, what are like the key principles? Again, we talked a lot about transplant. I think... I don't think you want to talk about transplant anymore and that's okay. Age alone shouldn't exclude people from treatment. So, I think it's great your dad is almost 90. My dad was 90 when he

started his treatment. So and he was a robust guy. Other people so (inaudible 2:44:22) is really that like you're "too old to do this," you need to reevaluate and be able to quantify why one treatment may be excluded or included for an individual or not, but definitely not age.

Q81: How did your dad do?

Jean Ridgeway: How did my dad do? My dad did okay. He also had another malignancy though. So, he passed from his other malignancy. He had lymphoma. A question?

Q82: Would you just say the word allogeneic as opposed to autologous?

Jean Ridgeway: Sure. So, there's two major types of transplants. So, there's an autologous transplant where I'm my own donor. We don't do that in MDS. We don't do that in AML. We do that in multiple myeloma. That's a standard of care for anybody who has myeloma. They usually get about four cycles of some combination and then they get their own stem cells harvested and they get their own stem cells reinfused. People who have refractory lymphoma, a totally different disease, they also can get an autologous transplant. An allogeneic transplant is you're getting somebody else's stem cells. That somebody else may be your sister, maybe your brother and that's called a matched related because I'm related to you. You're my sister. I get... We have the same mother and the same father and so it's interesting so when a patient comes in this is just done standard. There's no bias here, but a patient comes and they're 75 or younger to us and they have MDS one of the first things we do is we ask them about their brothers and sisters but you all have to say is it the same mother and father because... genetics says that here's me and so I had a mother and I had a father and so my genetic material came to me from my and my father. Now if I had a step sibling, maybe we didn't share parentage in a mother, but the father would be different. So, how closely related I'm going to be to this person is only a half. So, they're called a haplo. So, my children get half of their genetic information from me and half of their genetic information from their father. So when we draw and we look at their genetics, we look at something called the HLA typing. It's found on the sixth chromosome. It's for lots of reasons, but the closest match my child is going to be with me is a half unless there aren't a lot of branches on the family tree then maybe it'll be a little closer.

Q83: Is your child (inaudible 2:46:56).

Jean Ridgeway: We use children all the time because there's some ethnic groups that have a lot of options and the International Marrow Donor Registry people of mixed races do not. So say if you're Tai and Caucasian it's hard to find those genetic matches and there are other people groups in the world that... and remember this is an international... we have a national marrow donor registry. They have an international bone marrow registry. So, being part of a registry is just that swab from the cheek and then so you become part of what's called Be the Match in the United States and so my information is in a registry... I've never been called. I'm willing to be donor, but I just have never had the opportunity because if they go... and that's a computer

match. So if my sister doesn't match me then what happens is that we go to the donor bank and we run something called a search

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So, it's just numbers and there maybe six out of six or eight of eight, ten out of ten depending on how well they're... what they're looking for. There's a lot of different variables, but say they find somebody and they're a perfect match. Then they'd have to have the donor and ask them if they're available. My sister says... or the donor says oh, my gosh. I'm having a baby. Okay. You're X'd off the list or they say yes and then that donor has to be cleared. Now, some people don't have a match in the registry. So, what do you do? And then you can look for cord bloods and so the pro thing about cords is that they're frozen. People donated them when they gave birth, but they're what we call low doses. So, it's not a big cell volume. So if you weigh 120 pounds it's not such a big deal but if you weigh 420 pounds, it's a big deal. So, the size different... those stem cells are going to have to repopulate and you may have a weak graft or there could be some. So another thing that some centers are doing, they do only haplos. So, I have my sister's cells so they use that as an allogeneic source or they do alternative donors and they do something called a haplo cord. So, they use my sister and you use an umbilical cord. So, why do you do that? The biology is sometimes the haplo takes a one time to engraft so that means before you start making blood cells, 30 to 60 days before there's maturity to the point where the person has white cells, red cells and platelets. So, during that period, you're very vulnerable to infection because you have zero neutrophils. Cord bloods on the other hand... No, I'm going to flip that. The haplos engraft early. The cords engraft late. So, the cord blood actually engrafts at about 30 to 40 days. So if you do a haplo cord, the infusions actually happen on the same day and we look for the haplo to engraft by about day 11 to 14 or two weeks after the infusion, but because it's only a half a match, oftentimes the haplos don't... they don't stay with you and you lose the haplo whereas the cords will stay with you but they engraft later. So if you were a math person, you would say that engraftment from that haplo is earlier then it dies out. Engraftment from the cord is later and then continues so that you're covered during all of those times. So, the world of allogeneic transplant is... it's very complicated from a biology and an immunology perspective, but there are a lot of options. When people talk about an allogeneic transplant, it's very complicated and so if I do end up with someone from the registry, (Attendee) is my donor. I would be considered... they call it a blood transplant, a matched unrelated donor. So, that's coming from the donor registry. You hear MRD, you hear MUD, you hear haplo. You hear all these acronyms, so that's the difference. So, auto is cells, allo is another source.

Q84: But when you hear bone marrow transplant, you'd say but which kind are you talking about because it's just (inaudible 2:51:06) when it's your own...

Jean Ridgeway: Oh, my gosh. So different and actually nobody... there are very, very few instances that we truly do bone marrow harvests anymore. They're all peripheral blood. So if I became a donor, I got cleared. I would do Neupogen injections to myself for about four days and then I would go to the designated center and have a process called a pheresis done. If you ever

given platelets, you take the blood out and the blood gets spun and it's all done by weight and then the stem cells are collected and then the blood is returned. So, they take all your blood volume and circulate it through your total blood volume about four times and then there's a bag that hangs and it looks like a blood transfusion. The vial is about 200 milliliters and then that gets taken off to the cell lab and (inaudible 2:51:51) and stuff like that and being on the machine is about six hours for a single day collection.

Q85: Being and having MDS, you can't donate things like that.

Jean Ridgeway: You are correct. You would get things from the transfusion, out with you.

Q85: Being diabetic (inaudible 2:52:10) for like three times before I was actually diagnosed. I went in and just they'd say well, your blood's not good enough to collect.

Jean Ridgeway: And drop it in that little vial. You ever see them do that? (inaudible 2:52:22) things are slim. Right?

Q85: Well, I don't know if they did I, but it was frustrating because they'd go through the process and they'd prick your finger and you'd fill out all the paperwork and they'd say no we can't do it. I have a question on umbilical cord blood and they don't have a lot of it stored, but it isn't a very easy thing for somebody when they're going to have a baby to donate?

Jean Ridgeway: You would think, but it's very expensive. Someone has to absorb the cost and it has (inaudible 2:52:50) involved. They're little (inaudible 2:52:53) and there's a cost involved. So, some people do bank their own cords. Especially if you're a family member of someone with a blood disorder. If somebody's pregnant in the family that's kind of like the antenna goes up and they're like, oh, I'm going to bank the cord. So, there's an initial charge and then there's a fee for storage, but there are companies in the United States that also they procure them and I think that their linked with OB offices and then the woman signs a consent and then when the baby is delivered then they take the blood from the umbilical cord and store it. So, there are a number of companies.

Q85: So, you're saying that's all the mother of the baby is responsible for paying for that?

Jean Ridgeway: No, if you volunteer to donate your umbilical cord, there's no cost at all to you. You do have to sign a consent and agree beforehand. You can't... It's got to be a fresh collection and so that's what I mean about organized. So, then that company has... however the magic happens that a lot of things are going to get orchestrated, things are a little unpredictable. They come when they want to come and so there has to be some organization between the delivery site and the mother has to be consented and some centers do it better than others.

Q86: Now, you're talking about the bone marrow... They say it's a high risk of getting infection. What about the person that is giving you the bone marrow?

Jean Ridgeway: So, the risk of infection really doesn't have anything to do with the reinfusion of the stem cells. The risk of infection is now your body has to be your body's immune system and everything that recognizes a foreign invader in your body that all has to be suppressed. So, the main regulators in our body that do that are something called T cells and T cells are everywhere and so what's done is before someone gets a stem cell transplant, they're given chemotherapy for a couple of reasons. Many times it can be for further disease control, but it also preps the bone marrow to be able to take the new stem cell and allow it to implant like in fertile soil and grow, but in order to do that my body's immune system if you put somebody else's cells in my body the first thing that's going to happen is that my body is going to recognize it as foreign and it's going to do everything in its power to destroy it. So, what we have to do is take my immune system and give it medications to suppress the activity of the T cells and that's what makes people chromosome (inaudible 2:55:31) because you have to be suppressed enough to allow the acceptance of the graft and oftentimes people are very cytopenic during that time, low with the white cells and so there can be the possibility of picking up any number of infections. Dr. Sekeres said that (inaudible 2:55:49) was one of my patients and actually died from complications of a common cold. He had something called an RSV infection. You hear about that all the time. Kids get that and so that's the extent of immunosuppression and the inability to fight infection that can happen after transplant.

Q86: That's what we're nervous about now is where does the blood cell come and winter coming up. It's like now...

Jean Ridgeway: So what to do to protect yourself? Wash your hands with soap and water if you have soap and water available. Otherwise, Purell is great. Sick people should go away.

Q86: How about the flu shot for MDS patients?

Jean Ridgeway: Everybody should get a flu shot. The flu shot is a dead virus. So, it's not activated. Studies show though although it's not perfect, it decrease the amount of colds that people get and especially anybody who's in the immediate sphere like living in your house or you're close... everybody should get a flu shot.

Q87: The patient themselves?

Jean Ridgeway: The patient should get flu shot. Just they should not get the shingles vaccine. That's a live vaccine. Now, sometimes people do that. So, if I'm immunosuppressive and my husband gets the shingles shot, is that a bad thing? The only way it's contagious is if he develops

the vesicles, you know, the chicken pox looking things. If there's none of those he's not shedding the virus. So, it's not contagious, but the person themselves shouldn't get it.

Q88: After transplant, are you on medication for the rest of your life?

Jean Ridgeway: You get a lot of medicine. If you're getting an allo transplant, for the first six months you're on a number of different combinations of medicines and then things get weaned off and then you're off. So, not forever.

Q89: So, are you saying that we shouldn't maybe get...

Jean Ridgeway: Shingles?

Q89: Yeah, the shingle shot.

Jean Ridgeway: It depends. I don't know if you're neutropenic or not. If you're... the indication is if you're over 60 to get the shingle shot. You should all get something called TF. That's the booster for tetanus, diphtheria and polio. It's the new recommendation is once in a lifetime booster after the age of 20 which we all are, I think, but you have to really look at your blood numbers to see.

Q90: Talking about all this information or lack of information that's on, I'm just curious, how many people have read Robin Robert's book or are aware of it? What do you think of it?

Q91: I think it's very helpful.

Jean Ridgeway: Was it?

Q90: I want to highly recommend it and then she was here I would thank her for making it so public because it's created so many more donors for the list.

Jean Ridgeway: Absolutely.

Q92: And then the Tom Brokaw program, I think he had multiple myeloma. Tom Brokaw?

Q93: Yeah. He's on the Revlimid (inaudible 2:58:51).

Jean Ridgeway: He has multiple myeloma.

Q93: So, he's in remission, but he's not cured.

Jean Ridgeway: So, that's another "incurable" illness, but it's very treatable and people live with multiple myeloma many times like you do with diabetes. It's treated as a chronic illness. It can be more complicated than that. I'm making it very simplistic.

Q93: Developed a good program that he did (inaudible 2:59:16) a program that was on with him narrating it.

Q94: If the donor of the bone marrow, it doesn't bother them? It doesn't affect them at all.

Jean Ridgeway: Correct. It has to be safe. So one of the screening things that's done is once the donor is identified they have to go and be cleared by... there are certain physicians that can clear the donor. So, they undergo full evaluation including a chest x-ray and an EKG and make sure... it is interesting that some of the people I work with are looking into like genetic problems as well and we've had more than one donor turn out to be somewhat cytopenic, just like a little bit anemic or their platelets were a little low and they also been diagnosed early with a bone marrow disorder as well.

Q95: What about the pneumonia?

Jean Ridgeway: What about the pneumonia shot? Yeah, you should get a pneumonia shot.

Q95: Just I thought shingles just happened this week. I've had the low white blood counts below two and developed the rash and the shingles, but I have had the (inaudible 3:00:32) medication right away. So, it was a benefit to have had the shingles.

Jean Ridgeway: What happens as we age, we begin to lose some of that memory and robustness in our immune system. That's why a lot of times you hear about "older" people get shingles and so but the best thing to do is if you recognize a funny rash is just give your doctor a call and say (inaudible 3:01:02) funny little bumps, you should have it evaluated.

Alright. It is quarter till. Ten minutes and we got to go. Good? Because I have to catch an airplane. So, they usually don't wait for me. Earlier in the summer I broke my foot. So, I was going someplace and my foot was killing me. So, I went and I sat a far distance away from where my gate was and darned if I didn't miss the flight. I never heard them calling my name or anything. It was very funny.

Q96: How'd you break it?

Jean Ridgeway: Something big fell on my foot and broke the metatarsal but it's all better now. I missed the flight (inaudible 3:01:58) name, last call, the door is closing and I showed up and she goes, "Do you think we're waiting for you?" (inaudible) but that didn't happen. So good things to do to so if you need to be someplace and it's super public... I wouldn't say go a baseball

game. You just got to be smart and wear a mask. So, why is (inaudible) just a little timeslot thing. So, this first slide just shows that there's lots of bone marrow involvement and then what we're trying to see here is that here is the treatment course on the bottom. So if people start their treatment, here's their absolute neutrophil count. It may be higher and then a couple weeks into treatment it drops, but it will recover afterwards as the bone marrow gets a little bit healthier. So, this is a picture of... See these yukky cells? They're really abnormal cells. Those are dysplastic cells and then they get treatment, things kind of clear out. In general, there's not a lot of cells, but when things recovery the (inaudible 3:02:58) cells are gone and then you just have normal cells and growth and recovery with normal cells. So, that's what's going on and look who's name is on it. So, that's what happens. It's just kind of a picture worth 1,000 words, but this is the part that can be difficult getting through these first couple of cycles. People get discouraged with low counts, they still need transfusions, they don't really feel well and it's hard to see the light at the end of the tunnel when you're just crossing the threshold. So, and these are just... this is where you really have to work together with your providers when the treatment is first initiated and then this is (Name) over here two or three years into Vidaza treatment. So, I have a patient that's five years on.

Q97: Oh, really?

Jean Ridgeway: He's 75 now. He's an engineer. He still works fulltime.

Q98: Did you drop at first, (Attendee)? I'm sorry to interrupt.

Q97: Sure. I dropped. I think I was the lowest at about three months and then it just (inaudible 3:04:00).

Q98: We're at the low point now with my dad, really low...

Q99: Neutrophils when to .4 at the lowest.

Q98: He's at like .8 now.

Jean Ridgeway: Did you ever have problems with infections during the early treatment? Never hospitalized? Sometimes people end up in the hospital here. The most common times you really get very ill can be oftentimes at the (inaudible 3:04:24) treatment.

Q98: And it's stressful for the caregiver. You haven't said anything caregivers here because when you're told that if there's a fever of 105, you have to be in a medical facility within 30 minutes. I mean, that's a little stressful. So, the caregiver goes through maybe more than the patient.

Jean Ridgeway: True.

Q99: Your adrenaline spikes.

Jean Ridgeway: Absolutely. That really is the rule of thumb across the country, 105.5 and 30 minutes in.

Q100: Doing things like having paperwork on your that... I mean, you have to know these terms. The pancytopenia and that kind of thing helps the medical people, but also... I mean, even today I think I got my cipro with me (inaudible 3:05:18) someplace where you can't get him some help right away which is an antibiotic that the doctor prescribes prophylactically in case...

Q101: Is that like for a bladder infection?

Jean Ridgeway: You can use it for a blood treatment. The one thing that we worry about is the type of infection that's going to get people into trouble. There are certain types of organisms. Oftentimes people are getting something to cover a certain type of organism and it's more of like... it's just a protection.

Q100: I never used it without calling the doctor first because they would rather treat you for something specific, but if you're in the middle of nowhere or whatever it's helpful to have something like...

Jean Ridgeway: And one thing that I tell my patients when they come to the clinic is that you should kind of have a little bag in the car, have the names of your medicines, the names of your providers, a thermometer and if you're somebody who potentially start off with like nausea or diarrhea make sure that you don't leave home without it because if you're at clinic and you have trouble or if you're at someone's house and your life can be difficult, but I think that you just need to be proactive and things.

So, this is one Sandy Curtain's patients. So, she's one of the other nurses on the board and she worked with a doctor Alan List and Alan List did the original studies with 5Q- and Lenalidomide and so this is one of her patients that went through so you can tell that this person... so the orange... orange is platelets and then the pink is hemoglobin. So, it's just kind of graphing where this person's hemoglobin, so you can see there's a pattern to it. They get four cycles of treatment and they did go to transplant and then here's their counts after transplant that represent the function of their new hematopoietic system. So, they kind of like bounce around. Platelets drop, they go up and down, they really improved quite a bit towards cycle three and four. The hemoglobin stays relatively... it went from 12 to 80 and followed the little pattern. So, that was that person. This is a person who's been on treatment for over 10 years. So you can see, again, hemoglobin, he was pretty low when he started in (inaudible 3:07:40), but now he lives here about 12 and 13. This is platelets. So, his platelets really hover between 100 and 120 and then this is his white count which never gets super robust. Normally, it's between three and a half and

11, but for him he's reestablished a new normal that he lives with and stays on the drug. So, he's been on this medication for 10 years.

Kind of in closing, what can you do to stay healthy? Things that if you're not aware of already. You might eat a balanced diet. You can talk to (Attendee) about all the chemicals in life that she wants to eliminate but there's a lot of (inaudible 3:08:21) that when people say well, is there a diet I can eat to improve my counts? Unfortunately, there really is not, but I think if you can eat food that's related to nature, you're probably getting better nutrition than not. So, eat more kind of whole food kind of thing.

Q102: There's a new book out about (inaudible 3:08:42) your gut and probiotics...

Jean Ridgeway: And the microbio... that's the newest flash you'll see all over. We're realizing that the bacteria that colonize our GI system is helps... really helps in our immune status as well. That's why probiotics... There's a ka-billion studies out there about probiotics. They're not healthy. They're just not regulated. So, there's quite a bit of variability about what's available in them.

Q103: I've heard that they were dangerous to take if you were really neutropenic.

Jean Ridgeway: There's no data to prove that, but that's kind of the urban myth that's out there. Not knowing exactly what's in it. I have patients that take them and honestly I think they do better.

Q103: You do? Is that Culturelle?

Jean Ridgeway: Oh, they take them... There's so many different ones. I can't tell you what they take. Everyone has their personal favorite.

Q104: I didn't hear what (inaudible 3:09:33) said.

Jean Ridgeway: She had heard that there was some danger in taking probiotics if you're neutropenic and there's not a lot... there really isn't a good study to point to this data if that's true. People can take it or not. Remaining (inaudible) you might do as you want to do and do it well. Get enough rest and then you've got the resources, ask for help. Those are all good things. I was going to link into this, but I'm not going to do it. Partner with your provider and, again, I would say if you don't like your provider that's okay. You are not married to this person. If you want to go seek a second opinion, do. You're not going to offend anyone. You can fire your provider. Physicians are just humans. Some are better than others and make sure you can find yourself a good one because there's a lot out there and they can... Sue can help you find a good one in your area that will be a good fit for you that really knows about MDS. This is... it's

global, it's online. We talked about that already. It's interactive. They have questions. If you go on the website on a daily basis, there's questions that are posed by people.

Q105: Patient forums.

Jean Ridgeway: Patient forums and method for it and people chatter back and forth. This morning there was someone who was like... (inaudible 3:11:02) was just diagnosed I think with a myeloproliferative disorder and they were asking about (inaudible) 2 inhibitors, Jakafi and stuff. So, there's lots of different ways you can use this. You can track your progress, you can go online and track your progress, make copies by the book. It's not copyrighted. There's lots of links as well. In the PDF, you can put it on your iPad or your Kindle, but you can't interact with it, but you can at least have it at your fingertips if that's what you like to do and lots of advocacy. You're talking about Epogen before. CMF which is the government arm of Medicare that helps... that decides what they're going to pay for or not pay for wanted to remove Epogen from MDS and not allow patients who had MDS to receive it as a treatment and it was patients that went to Congress and lobbied to continue it that have allowed MDS to continue to be able to use Epogen and Darbepoetin as a therapy. So, it really does pay to get involved and let your voice to be heard. We pay those peoples' salaries. So, they should listen to what we have to say and this is just more about the book how you use it, etc. and then about the Foundation as well and that's all I have.

Q106: Can I just thank the Foundation.

Jean Ridgeway: Absolutely. They do a wonderful job.

Q106: The book and the new book with the 100... thank you so much and we all get solicitations from the American Heart Association and this, that and the other, but I figure this is where we need to be donating money because if we don't do it, who's going to do it? So, think about that in your charities.

Jean Ridgeway: So, what can I say? Thank you all for coming. I hope you gained at least one piece of information that could be potentially useful for you after today.