



Speakers:

Alison R. Walker, MD

Jean Ridgeway, MSN, APN, NP-C, AOCN

Alison R. Walker, MD: Like I was saying, my name is Alison Walker. I'm one of the hematologists over at the James and I wanted to thank the Foundation for the opportunity to be here this morning. I did spend some time with you. What I'm hoping to do really is talk with you a little bit about some of the things that are coming down the pipeline in terms of treatments for MDS, but then also really give you an opportunity to ask any questions that you might have. I've got some PowerPoint slides to help along with that. I think we're trying to work on doing that.

I have a couple of questions just because I'm going to be talking about some clinical trials that were presented at the American Society of Hematology which is our national meeting where we learn a lot about and hear about research that's being done whether than be in Europe or in the United States and so it's a time when researchers like myself present their data to large numbers of us and it's nice to be able to come back home and to share that information with our patients and so I'm just curious how many people here have participated in a clinical trial? Just one. And so maybe while because I'm going to talk about a couple of different things related to different phases of clinical trials, I'll just mention that briefly and forgive me if this is something that your doctor has already talked with you about.

So, any drug that comes to market initially starts out in what we call a phase one clinical trial which is being done just to assess how safe and tolerable a single drug or a combination of drugs might be for a particular group of patients. We never do phase phase one clinical trials without on the backend trying to figure out how well it works, but that's actually not the goal of a phase one trial. We first want to see if people can even tolerate the medicine and then escalate that to the highest dose and I mention that because I think two or three of the trials that I'm presenting that were discussed back in December at our annual meeting were these phase one clinical trials for patients with MDS. After a phase one clinical trial, after researchers have determined what's the safest and best tolerable dose, we move onto what's called a phase two clinical trial where we take that dose we've defined and we expose 30, 40, 50 patients and we see well now how well does it actually work in a bigger number. Phase one trials can be anywhere from nine to 15 patients. They're not very large and so it's hard to say, "Well, oh, this will be the response that you get when you actually give the medicine to a larger group of patients," and then finally... well, not finally, phase three trials are when you take this new agent that you've gone from phase one to phase two. You've gotten a really great response and you say, "Okay. Let's compare that new one that we've defined or found to what our usual thing is that we normally give patients," whether in the case of MDS, say, it would be Vidaza or Decitabine, but we've got this new drug, Axim, we're going to compare that and patients are actually randomized to receive either this new and improved, we think, therapy or the standard therapy and then we look at some long term outcomes and determine which one's actually better. Is there any survival benefit, those sorts of things as well as side effects and so those are the different phases or clinical trials and so we're going to be talking at least about phase one and phase two when the slides come up. Otherwise, I

can just kind of describe them to you and you all can just look at me which is always a little bit (inaudible 4:27). Any questions about that or does that make sense?

Q1: (inaudible 4:30)

Alison R. Walker, MD: So, the James... I work at Ohio State. The James' are comprehensive cancer center where one of, I think, 12 or 13 (inaudible 4:49) at cancer centers in the United States with a specific NCI designation and so that's where our patients... our patients have a separate hospital from the... it's not separate physically, but it's... well, not yet because we're building a new cancer hospital which will be open in, I believe, the second or third weekend in December, but we have a specific James Cancer Hospital where our patients are treated, clinical offices where patients are seen. So, it's a little bit separate from the main hospital. Who here is from Columbus? How about other places that people are from? Yeah. It's funny because I'm looking like you look familiar. Maybe I passed you in the 11th floor waiting room or something like that.

Q2: (inaudible 5:36)

Alison R. Walker, MD: Anyone from Cleveland or Akron or Dayton or anything like that?

Q3: (inaudible 5:50)

Alison R. Walker, MD: Sure. Absolutely. Oh, sure. Sure. They do great work there. Yeah. They're a great team. From where?

Q4: (inaudible 6:03)

Alison R. Walker, MD: How far from here is that?

Q4: (inaudible 6:08)

Alison R. Walker, MD: From Dayton. Say it again.

Q5: From Dayton.

?: You have to push the button.

Q6: I'm from Greenfield, but I have Dr. (inaudible 6:36) and I can work through you and the doc.

Alison R. Walker, MD: I was going to say are you going to say something either nice about your doctor at the James?

Q6: Yeah.

Q7: I'm from Toledo, Ohio and seeing a hematologist there.

Alison R. Walker, MD: Are most of you patients living with MDS or caring for patients or who has or...

Q8: We have it and I have it and we're from Pittsburgh.

Alison R. Walker, MD: From Pittsburgh. Oh, okay.

We can just talk a little bit and if there are any questions on your mind right now otherwise I think we'll... Sure.

Q9: Do you have to be like higher (inaudible 7:34).

Alison R. Walker, MD: That's a good question. There are some clinical trials specifically for patients with lower risk disease and so usually when I'm meeting with a patient and we're going through their bone marrow biopsy report and their labs and we're trying to figure well, what do we do? We talk about where they fall in terms of their risk of low risk, intermediate and high risk and so a lot of trials tend to be more so for higher risk patients typically because they involve chemotherapy or the consideration of transplant and things like that which for lower risk patients isn't something that you always consider upfront. There are... Oral Azacitidine is an agent that is in clinical trials that is specifically being looked at in patients with lower and Intermediate 1 risk disease. Sometimes the trouble with clinical trials and it isn't because we're trying to not give someone some new therapy, but it's more to make sure that we're not exposing patients unduly to risk and making sure that they're appropriate for the clinical trials. So, there are all of these inclusion criteria that you have to meet and sometimes I meet with patients and we go through the list and then we get to one which is something that, unfortunately, prevents them from participating in the clinical trial, but it's really just more for patient's protection. Oh, that's wonderful. Thank you so much, sir, in the back. I appreciate your help. So why don't we go ahead and... unless there are other burning questions right now and I don't really have too many slides, but just to like I said talk to you a little bit about some of the things that were presented at this year's annual meeting that I thought might be of interest because I should mention that I mostly take care of patients like yourselves, patients with MDS and acute leukemia. I am not a transplant doctor and so a lot of the conversations or most of the conversations I have are about what treatment do we do next and I don't have to tell you that it's not like your doctor has a laundry list of different things that they're able to try and sometimes that can be frustrating. So, I thought that this might be something just to kind of keep your head up about things that are coming down the pipeline that it may be at some time but something to kind of hear about. So go ahead and get started.

So, I'm first going to talk about nontransplantation strategies, again, because I think that that's more applicable to the majority of patients. At least the patients that I see, but we'll talk about a couple of transplant trials that were presented as well as talk about at the end some trials available at my facility, at the James.

So, this first clinical trial that was presented was actually an oral presentation which is a big deal. So at the meeting, you either are someone standing up in front of a very large room presenting your data or you're standing in front of a poster sort of presenting your data and that's really how we go around and kind of learn about the different things that are going on and so this was actually an oral presentation at this year's meeting and it was a called a Phase Two trial of a Genetic Modulator, Vorinostat, in combination with Azacitidine in patients with Myelodysplastic Syndrome and this was actually a group out of New York. This is a very exciting trial because Vorinostat is actually an FDA approved medicine and so a lot of drugs that are in clinical trials about development can be something that a drug company is sort of working on in their pipeline not something that the FDA has approved for someone to give and so Vorinostat is actually an FDA approved drug for the treatment cutaneous T cell lymphoma. It's an oral agent. The most side effects tend to be things like diarrhea, fatigue, nausea, blood count changes like thrombocytopenia, decreases in appetite and some taste changes. The mechanism of action of this agent as it applies to MDS is that it affects and targets abnormal gene activity within cells and so although we don't know exactly why MDS happens or what is going on exactly in the bone marrow, we think that part of the problem is that the genes that should normally be telling your bone marrow to make white cells, to make red cells, to make platelets to not make blasts, those genes are disrupted and their activity is aberrant and so we think that Vorinostat helps to re-equilibrate that and sort of get the genes going in terms of doing what they're supposed to do. This agent, they believe, acts very similarly to Vidaza or Azacitidine and Dacogen or Decitabine, but in a slightly different mechanism and in a phase one trial as a single agent just alone, they found that about 20 percent of patients with MDS had an improvement in their abnormal blood counts and so sometimes medicine can be simple and you say, "Well, if it works by itself in this group of patients with MDS, what if we were to combine it with what we're normally giving patients and maybe we'll get some added benefit," and that's just what these investigators did. So, this trial included patients with Intermediate 1, 2 and high risk disease. They're not patients with low risk, but INT1 and 2 and high risk, they gave a little bit of a different schedule, the Azacitidine. Who here has ever been on Azacitidine before? It's usually about a week long of treatment that you receive and so they did it for about the same amount of time, but they adjusted the doses keeping it the same as it is what we would normally give, but then also slightly a lower dose and then they change the dosage of the Vorinostat that they gave and that's a very standard procedure on clinical trials.

Q10: (inaudible 13:10)

Alison R. Walker, MD: Yes, it is

Q10: (inaudible 13:13)

Alison R. Walker, MD: Okay. I'm sorry.

Q10: (inaudible 13:16)

Alison R. Walker, MD: So, there were 40 patients that were enrolled, 21 men and 18 women. Most of the patients had higher risk disease. So, Intermediate 2 or high risk in the median age is about 67 although there was a range that you can see listed there and interestingly the overall response rate for 33 patients that were available was 70 percent. So, that's higher than we would expect for Azacitidine or certainly for Vorinostat alone and 10 patients were actually able to achieve a complete remission. Four people had what we call a complete remission with incomplete counts and what that means is when we do the bone marrow biopsy, really we don't see any evidence of the dysplasia or any abnormalities in the blood cells. We really don't see any increase in blasts, but the blood counts and platelet count maybe it's still 50,000 or maybe your absolute neutrophil count, that's probably something your doctor talks with you about, it's still only about, I don't know, 800. It hasn't reached the official levels in order to sort of qualify by the book for a complete remission and then 9 patients actually hematologic improvement and while that's not a complete remission per se, that's still relevant. So for example if you're a patient who is requiring transfusions all of the time, once a week, twice a week, but say your bone marrow doesn't get better but you get a point where your quality of life improves because you're not having to go to the doctors once a week for a labs or getting transfusions. That can be a big improvement for patients and it seemed like the highest response rate was in patients who received the Azacitidine at a slightly lower dose than we normally prescribe in combination with the Vorinostat, 200 milligrams twice a day.

So patients received anywhere from one to 26 cycles and that goes along with the idea that Vidaza that... or Azacitidine that people are on. As long as it's working, your doctor probably tells you we have to continue it for fear of stopping and having things revert back to the way they were before. The median number of cycles that people receive was about 6 and the most common toxicities were toxicities related to the Vorinostat that I mentioned previously in the first few slides in terms of fatigue, vomiting, diarrhea, dehydration and then just looking at the median overall survival for this group of patients was about 21 months and so it's important when you look at that number to remember and to keep in mind that this was a mix of people with different varying degrees of risk and so the median is always that 50 percent point. So, 50 percent at that point 20... the overall survival was 21 months, but 50 percent of the group lived longer than that and the 50 percent of the group, of course, ahead a shorter survival than that and interestingly thee patients were able to use this as sort of something to move on to transplant from. So, showing that it is an effective regiment from that standpoint.

So, the conclusions from this study and, again, it's a phase one study was being done to (inaudible 16:14) how safe and tolerable something is. The conclusion was that this was a safe and tolerable dose. They identified the maximum dose. The mechanism of action, again, behind why exactly the combination of the two drugs is more active isn't clear, but that's something that

they're working on and trying to explain in the lab and also what's interesting is that this clinical trial is ongoing and it's going to be part of or is part of a larger intergroup trial where they're comparing this combination versus Azacitidine versus Azacitidine plus Lenalidomide and so that's something that is ongoing right now. I'm sorry not phase one. It's phase two. Yeah.

Q11: So, at what point do positive results that you just pointed to turn into a best practice? At what point do they say okay, this is something we're going to start to implement?

Alison R. Walker, MD: Yeah. A long time. Unfortunately, it's a long time because what the FDA will want is a large phase three randomized trial comparing this combination in a large group of patients to Azacitidine and so and that can take years and they'll want to... There's some specific requirements by the FDA in terms of what amount of a survival benefit or response benefit they'll want to see. A little bit, unfortunately, is business. So, the company that makes this might say okay, sure. This is going great, but a year from now what if their company is not doing well and they decide okay, this isn't a large enough... MDS isn't a large enough market. We're not going to support... and so it can be complicated, but it's not something, unfortunately, where you could go to your doc Monday and say, "Hey. We got this and this is FDA approved. Can you combine these together?" It's just not... There's not enough data to do that and it's not safe yet, too, because we want... This is all very early information and as a clinical researcher, we have all seen cases where initial information is presented at this very important meeting and then a year or two later you find out oh, this happened or actually when you looked three years in the future for all these patients it all kind of evened out. So, those are the important things and why drug development takes so long.

So, the next clinical trial I wanted to talk about an abstract that was presented at the meeting is a phase one dose escalation expansion study of ARRY-614 in patients with low or an Intermediate 1 risk Myelodysplastic Syndromes. So, this is actually an interesting agent. It's very different than the Vorinostat that I previously mentioned. So again, this is something that is not an FDA approved medicine. It's something that the company has in development. It works differently. It actually works to inhibit the activity of the abnormal proteins within the bone marrow environment. So, where the MDS cells are living because there's some idea that the environment where the cells are somehow interacts with the cells and causes them to do good things or bad things and so a lot of research is being done to look at how we can manipulate the actual bone marrow environment itself in addition to targeting the blood cells and so this particular drug actually allows red cells and neutrophils and platelets to live longer because part of the problem with MDS is that you have ineffective production of your blood cells. So, your bone marrow sort of makes them, but they don't live as long as they're supposed to and they sort of die off and then they don't get out into your blood stream and then when you get your blood count structure counts are lower. So, this agent is actually trying to help to mitigate that.

So, this was a phase one dose escalation study enrolling patients with lower and Intermediate 1 risk MDS and they did allow patients who had received prior treatments for MDS to enroll which many phase one clinical trials do and this is important because when you are looking sort of on

the back end and what's the response rate if you find that even if you see a little bit of activity or someone... a couple of people have some improvement in their blood counts or a complete remission or something like that, it makes you think, "Wow. This drug even worked in someone who had a lot of different treatments before," and so that's always something to consider. So, this trial is a little bit larger. It was 62 patients. Most of the patients had Intermediate 1, not too many had the lower risk and the median age was about 72, but a fair range up to 85 years and, again, the median number of prior treatments was four. So, that tells me when I'm reviewing this that this is a heavily pretreated group of patients where, gosh, I'm not going to have a lot of options. We may need something that's going to be kind of working from a different mechanism and how well will things work and so they actually because this was a dose, standard dose escalation, they looked at several different doses up to 1,000 milligrams once a day. The average or median duration of treatment was shorter. It was only about 13 weeks although there were up to 65 weeks. So, more than a year that some patients were on treatment and the most common symptoms that were noted were fatigue, rash, nausea and vomiting and appetite changes and then something called atrial fibrillation which is an abnormal heart rhythm which can be fast and sometimes people can be symptomatic from that in terms of chest pain or feeling their heart race or shortness of breath. Sometimes people are not symptomatic from that and that's usually something that can be controlled with oral medications, but for some patients can be more serious.

So interestingly, 12 out of 54 patients, so 22 percent had some sort of improvement in their blood counts by official grading criteria that we use and I've sort of broken it down here where six percent of patients had increases in red cell count. Twenty-one percent had increases in platelet count and I always feel like when I need to transfuse patients or, say, we're in a stage of their disease where we're not doing therapy and we're doing supportive care, I've always feel like red cell transfusions last longer for patients, but platelets... usually if you're platelet dependent you might be coming once or twice a week to have transfusions and so having a 21 percent increase... 21 percent of patients had increases and their platelet count tells me that this is a great drug even if, again, for quality of life, for maintaining their activity and able to do things at home and then, again, 12 patients who were transfusion dependent had a 50 percent decrease in their transfusion requirement, which again is an important thing for patients who do rely on transfusions and then the all-important increase in neutrophil count, 31 percent of patients... We know that the lower your neutrophil count is the higher your risk for potential infections and so being able to mitigate that somehow is certainly an improvement and what's, again, is very interesting from this agent and this abstract that was presented is that all patients who had achieved a response had received Azacitidine or Decitabine previously and just in general in practice when I'm seeing patients when someone has progressed after or has not responded to either of those agents, it tells me that their disease more aggressive and it's something that I'm concerned about for them in terms of what else I might have to offer and so the fact that this is an agent that works even in those groups of patients or in those groups of patients is very encouraging to me and so this is definitely an agent we'll keep an eye on and so for the most part the conclusions that the investigators made was that this was a well-tolerated regimen and they define what the maximum tolerated dose is going to be and again they're looking to kind of

explore this in patients with lower risk disease particularly those that have been treated with either Azacitidine or Decitabine. So, again, something that we'll wait to hear more about.

So, the next abstract that I wanted to talk about is combining Lenalidomide with intensive chemotherapy in people with higher risk MDS and deletion 5Q and this actually from the French group. So, has anyone here ever been on Lenalidomide or has that ever come up in conversations and things? Yeah. So, sometimes there is a little bit of discussion about what to do with higher risk patients particularly younger patients, 30s, 40s where you might want to consider or think about is there a role for it. Instead of doing Vidaza or Azacitidine, should you treat them with a more intensive IV chemotherapy in the hospital for four to six weeks, sort of regimen and this trial is sort of looking at that question in combination with Lenalidomide for a particular group of patients and so here in the United States, Lenalidomide is FDA approved for the treatment of patients with 5Q- syndrome which is a specific subtype of MDS. Typically, it's women usually in their 50s to 60s, although these are sort of generalizations, tend to have a normal white count, maybe a little bit higher platelet count, but do tend to have significant anemia and what they found though with this agent patients become increase their hemoglobin, become transfusion independent. This agent's also been used and it is approved patients with lower risk disease just in general although the response rates that we get in terms of the improvement in someone's anemia are less. It's about 25 percent versus about 66 percent when you treat patients with the 5Q- syndrome with Lenalidomide. It's a very, very interesting drug. As I mentioned, it's FDA approved here in the United States for MDS, but it's also approved for multiple myeloma. We've used it in AML. It's been used in different lymphomas and so its mechanism of action is likely multifactorial and that's something... It's an active area of basic science research, but there are a couple of things that we do know. It does appear to have some immunomodulatory effects on patients' immune systems and, of course, affects hematopoietic cells or blood cells within the bone marrow and we actually do think that it affects some of the proteins and how they break down within cells which can be important and particularly in malignant cells or cancerous cells because if you can figure out how to make a protein look bad to your cell and get rid of it, the cell won't be able to survive and it will die and so in a cancer cell if you can figure out how to make bad proteins look bad so that the cell destroys them and the cell dies that would be an advantage and we think that Lenalidomide does something with that.

So in this particular trial, it did include patients with Intermediate 2 and high risk MDS, but you had to specifically have a deletion 5Q whether that... it's unlikely that patients with a 5Q- syndrome were enrolled to this. Most of the patients had the deletion 5Q or chromosome abnormality in combination with other cytogenetic changes and so I just had a thought and I wanted to make sure that people understood what deletion 5Q or chromosomes... had you talked with your doctors about things like that. So, a couple... it looks like a couple of people have. So just very, very briefly. So when you have your bone marrow aspirate and biopsy done, they do the chip of bone and then they also take the liquid part and there are two things that they do with that liquid part. One, they look at the cells under the microscope and kind of look and see how healthy they are, but they also send a sample of that to the lab and they actually grow the genes, the chromosomes, in your blood cells and so not so much genes that you inherited from your

parents and that you would pass onto your kids, but genes that within your blood cells that have changed related to your MDS and so for some people, we see a lot of different sorts of changes and additional that, an extra this and where is that part of that and then some people it's normal and then some people there are some other changes that can occur and based on the changes that your doctor sees they can kind of classify you into low or intermediate or higher risk and the more changes and additional things and you've got going on or gene changes that are seen technically and usually the higher the risk is. So, there's a specific chromosome change called a deletion 5Q that can be picked up through this technique and so they identified patients who had that and enrolled them to those trials. So, I would encourage you to talk with your doc about did you have any chromosome changes or any gene changes with the bone marrow biopsy because that's something we consider when we're looking at treatments for patients and sort of long term survival and need for transplant and those sorts of things.

So anyway back to the abstract. So again, this was patients with higher risk MDS but also included patients with AML and they received a standard AML type induction chemotherapy. The first two agents, idarubicin and cytarabine are IV chemotherapies and then Lenalidomide 10 milligrams or 25 milligrams once a day and the patients who are able to achieve a remission could go onto then receive some additional chemotherapy and there are a total of 82 patients that are enrolled. The smaller... most of these patients actually had AML but there were 21 patients with MDS and the median age for the entire group was about 66 years and so overall about 46 percent of patients were able to achieve a complete remission and, again, five percent achieved a complete remission but didn't have their blood counts come all the way back up to normal and it didn't appear that their response rates were any different based on the doses that you received of the drug. So whether you received the 10 milligrams of Lenalidomide or the 25 milligrams of the Lenalidomide, a lot of times in clinical trials we use our best judgment and sometimes start at a lower dose. The next dose level is an intermediate dose. The next dose level is a slightly higher dose and that's just seeing and based on a very simple concept that maybe if someone receives more drug and they're able to tolerate it that that might be more effective, but interestingly they didn't really see any difference in the response rates, but was of note is that patients with MDS appear to have a higher remission rate than the patients with acute leukemia and whether that's related to the fact that the diseases are different slightly and more aggressive potentially with AML, it's not really clear, but something that this group as well as other groups have looked at and so overall about 72 percent of patients unfortunately who did respond to the treatment did relapse and the average time, median time, to relapse was about six months or so and there are a number of side effects. Five patients died early in due to infection. One patient had a heart attack. There are some other side effects that were observed in terms of changes and liver enzymes, kidney function, lung problems. This primarily has to do with the nature of receiving intensive chemotherapy not so much the combination of drugs. So when I'm talking with my patients who have had MDS that turns into acute leukemia and we're thinking about intensive chemotherapy like this, these are some of the side effects and so I wouldn't say that it's just because of the addition of this new agent that these things happen. These are standard things, unfortunately, and that's the high risk of doing intensive treatment.

So, the conclusion was that really the combination of Lenalidomide with chemotherapy did not appear to delay count recovery and their response rates were relatively similar, but it's very clear that we need further improvements in this regimen and others to help to improve the long term responses. I think that that's important because when you have three-quarters of the patients who still relapse at some point after they've received it, it tells us that maybe it'll work for a short amount of time, but there's something more than needs to be done.

So, I just have a couple of updates on bone marrow transplantation and then a quick slide about some of the trials that we're doing and then we can stop and talk. I don't know if anybody has any questions from what we just talked about here. Okay.

So, this I thought was interesting because they're talking about transplantation for patients who develop MDS after they've been treated for aplastic anemia with immunosuppressive treatment. This is actually a publication from Fred Hutchinson's group... the Fred Hutchinson Group in Seattle which one of the larger transplant organizations and so transplantation from MDS, it's not a common thing. Aplastic anemia is not a common thing, but the usual treatments for that disease which is a problem where your immune system attacks your bone marrow and so instead of having normal white cell counts, red cell counts and platelets, you know, you're platelet and transfusion dependent. Your white count is 0.1, your hemoglobin for platelets are 5. Your bone marrow is just not working because your immune system has attacked it. Just like immune systems like MS or immune diseases like MS or rheumatoid arthritis. You've developed sort of this immune reaction against your bone marrow and so the way that we treat that is with immunosuppression and usually that works pretty well, but there is this risk of the development of Myelodysplastic Syndromes in about 15 to 40 percent of patients and so this study was trying to look at whether or not patients who develop MDS after aplastic anemia how well do they do. Do they do any differently than patients who develop MDS out of the blue and then go on to receive a transplant? So, this looked at 123 patients between 1977 and 2011. So, just looking at that large span, you can tell that this isn't something that happens commonly if over all of those years they were only able to identify 123 patients. Eighty-nine had refractory anemia and 34 have what they termed advanced MDS and the median age is a bit younger than in some of the other trials that I've talked about and that was 28 years although a range of 2 to 68 years. Again, mostly because aplastic anemia tends to be a disease of younger patients, but some older patients that I care for (inaudible 33:45) in their 60s have been... I've diagnosed with aplastic anemia. Eighty percent of the transplants were from unrelated donor and interestingly there was a similar time to count recovery after a transplant. So, typically in a bone marrow transplant you receive some sort of... you come into the hospital. You receive X number of days, four or five, depends of some sort of chemotherapy and then on, call it day zero, you receive an infusion of your stem cells and then you wait and you wait for your blood counts to come up. You wait for those stem cells to engraft in your bone marrow to start populating and making your white cells and so one of the ways when they look at transplant trial is to see how quickly counts recover because the longer your counts are low the higher your risk is for any sorts of infections and need for transfusions and other sorts of problems and so they noticed that there was a similar time to count recovery after a transplantation. The rates of acute and chronic graft versus host disease

was similar and so, again, I'm not a transplant doctor, but my very simple explanation when I do have these conversations with my patients is say you need a transplant and I'm your donor, I'm the donor pool. I would happily donate to anybody. You would receive my stem cells that you would get my immune system. It would go into your bone marrow. It would make red cells, platelets, white blood cells, but you'd also get my immune system whose job is to protect me and they would float around in your body not realizing they're not in my body anymore, but float around in your body and say, "Well, hey that's not Dr. Walker's liver. That's not her skin. That's not her intestines. I need to attack that because my job is to protect her," and so that problem is something called graft versus host disease. So, the graft versus the host there's an attack by my immune system on your body just because that's its job. It's supposed to protect me. It just doesn't realize that it's in somebody else's body, but the benefit of my immune system is that it sees your blood problem as an abnormality and attacks that and gets rid of it and that's kind of how transplants work in a very, very, very, very simple sort of the way, but the problem is that that can cause your liver to abnormal and give you terrible diarrhea. It can give you a lot of rash and skin problems and so they judge something called acute which usually happens within X amount of days and then chronic is something that's going on for a long amount of time. So, they look at that and they saw that that was similar. So, no difference and then also the five year survival rates were also very similar which is also important as well and so that just, again, is showing the fact that patients who do have MDS evolving from aplastic anemia can have similar outcomes to patients who have MDS coming out of the blue and receiving a transplant.

This I thought was an interesting abstract because the title of which is Prior Hypomethylating Agents or Chemotherapy Does Not Improve the Outcome of Allogeneic Hematopoietic Transplantation for High Risk MDS. So basically looking at the question of I have a patient, I've determined... that myself and the transplant team, we determined that they're appropriate for a bone marrow transplantation and then they look at me and say well what are you going to give them before their transplant? Usually typically, I would use a hypomethylating agent. I would not... such as Vidaza or Decitabine. I wouldn't do intensive chemotherapy and this trial was actually looking at is there a difference in the long term. So do people who get Vidaza before a transplant do better or do people who get chemotherapy before a transplant do better? And so this is actually a retrospective study that was done and basically this is what I was just explaining and this looked at 291 patients with MDS between the years 2000 and 2012. One hundred seventeen had higher risk features including therapy related MDS. We know that MDS that occurs after a very appropriate treatment for breast cancer or a lymphoma or a prostate cancer that that MDS can be more difficult to treat and we also know that someone with high risk chromosomal abnormalities. So what I was describing before when they do the bone marrow biopsy and the aspirate and they look at the cells under the microscope and they grow the genes and there are all these different changes, those are higher risk chromosomal abnormalities. So, the median age for this group of patients was 55 although, again, a considerable range as young as 18 up to 71 and 18 percent of patients had received intensive chemotherapy. So like that idarubicin and cytarabine that I talked about on a previous slide, about 100 patients had received Azacitidine or Decitabine. Fifty patients had actually received both and 74 patients hadn't received any treatment at all and so interestingly there was no difference in relapse or death after

transplant between the group that got Azacitidine or Cytarabine are in intensive chemotherapy. What was also interesting was whether your disease was in a complete remission or not prior to transplant meaning you had your bone marrow before your transplant procedure was... you were supposed to go in and it looked great, no evidence of any dysplasia, no increase in blasts. It really didn't matter influence relapse or death after transplant but the most important factors were actually whether or not you had those abnormal chromosomes as part of your disease when you were diagnosed and then if you did not have a donor that was is more well matched to you.

I forgot that I had this in here. This is an update on Rigosertib, which this was not something that was presented at Ash. I believe it's going to be presented at ASCO, which is the American Society of Clinical Oncology and their meeting's in Chicago in end of May, early June. I think that's when the company is going to be presenting this data, but I wanted to present it because it's a phase three clinical trial. So, this was actually comparing this agent to best supportive care, that randomization, something that I talked about when we were first were waiting for AV things to get going. So, this is actually an intravenous agent and its mechanism of action is also a little bit different. It's not really affecting genes, but it's affecting sort of the signaling pathways or how the cell kind of communicates within the cell and basically it tends to promote the death of the abnormal hemata... blood cells and so it's been studied in MDS as well as head and neck cancers.

So, they randomized patients to either receive this agent or best supportive care and these are all patients who have been treated already with Azacitidine and Decitabine. So again, a population of patients where we really don't have outside of a clinical trial a lot of options for them. Two hundred ninety-nine patients were enrolled, 199 patients received Rigosertib and the side effects for the most part, this was a well-tolerated agent. Some nausea, diarrhea, fatigue, constipation, so kind of GI kinds of side effects, but there was no significant difference in survival between patients who received the Rigosertib or the best supportive care which would be things like transfusions of antibiotics and those sorts of things and this goes back to your question about phase three trials and when it's going to eventually get to where it becomes a best practice and this agent has been in development for some time. This was a phase three trial that their main result what they told the FDA that they were going to approve they didn't prove and so now the company is saying are we going to pursue this anymore? What are we going to do with this? And that's unfortunate because, again, there are more analysis that will be done, I think, with the data and with the company and things like that, but there did appear to be an improvement in survival for patients who had never responded to Azacitidine or Decitabine. So usually, we do Azacitidine for four to six cycles. If we don't see some sort of improvement in blood counts, decrease in transfusion requirements, we stop because it's not effective and this drug looked like it might work just in that group of patients and so my hope is that when they present this data in June that maybe they'll have identified some other things. This was just brought up. I think there was a press release in February of this year about these results and so I think there's probably more to the story coming with this, but just kind of getting to the fact that how some things can get to this point and still not maybe make it to patients just yet.

And then I just wanted to talk about one clinical trial at the James because even though I'm not a transplant and I do see patients with MDS and a lot of times a transplant question does come up and this is really exciting because it's a multi-center biologic assignment trial comparing reduced intensity allogeneic transplantation of hypomethylating therapy or best supportive care in patients 50 to 75 with Intermediate 2 or high risk disease and so just to break down the terms a little bit. So, biologic assignment means if you have a donor then you would be someone that would be potentially randomized to receive a transplant. If you had no donor whether that you don't have any brothers and sisters, they've looked electronically in the National Donor Registry and there are no potential donors there. They've looked in the Umbilical Cord Unit Registry. There's nothing for you there. So biology assignment just means whether or not you have a donor identified or not and then patients will either receive hypomethylating therapy. So the normal therapy that we would normally give somebody or best supportive care for patients with higher risk disease and, again, emphasizing 50 to 75. So a lot of times when I'll see patients in consultation and they're coming from somewhere they don't have a clinical trial like this or consideration of a transplant is something that we will talk about and so this is usually something that I work closely with Dr. Vasio (sp? 43:20) who's one of the members of our transplant team and we sort of coordinate. As soon as they have an appointment with me they usually have an appointment with here and kind of meet and kind of get started with the process if they're interested so and this is something that's actively open right now here at the James. So and I think that's my last slide. Thank you so much for your attention and I'd be happy to answer any questions and hopefully I didn't talk for too long. Sir.

Q12: I want to go back to the first part. (Attendee) has been diagnosed with low risk MDS. She's been on Aranesp for eight months. Our hematologist is suggesting that it's not working because it's not raising upper levels. It's pretty much staying level and they just took her 500 milligram dose and increased it to every two weeks. If that doesn't work then he's suggesting the Lenalidomide and a clinical trial. It's a new one that's a variation of that. Are you familiar with that at all?

Alison R. Walker, MD: No. Is it Pomalidomide or what...?

Q12: Don't know the name. I just wondered if you...

Alison R. Walker, MD: Oh, sure. No, no, no.

Q12: Do you have any knowledge of how the gene therapy is working with the modified T cells?

Alison R. Walker, MD: Sure. So, I think you're referring to Cartese (sp? 44:44) which are chimeric antigen receptor targeted cells. This is work that's been primarily out of the University of Pennsylvania, Dr. Carl June, as well as investigators in New York and essentially to my knowledge all the trials have really been looking at and enrolling patients with acute lymphoblastic leukemia and AML CLL. I'm not aware of any patients that have been... with MDS that have been treated on any of those clinical trials. I don't think that's been work that's

been done yet. We here in Columbus at the James were actually in the process of the long approval process of a clinical trial with a cartie (sp? 45:27) and doing that processing and things like that for patients with acute lymphoblastic leukemia or ALL, but I'm not aware of any work that's being done with MDS yet and the only thing sometimes with myelo risk patients if we're doing Aranesp injections and typically the average that that will work will be about a year, a year and a half and sometimes longer is I'll try combining that with Neupogen injections and sometimes that can increase someone's hemoglobin and support them through with... before having to get on some sort of active treatment. So, something to think about, but... and a clinical trial is always a great option if there's something like that that's available.

Q13: Yes. I was wondering on that 75 with the bone marrow transplant it said that they received no chemotherapy or anything like that. Was it they just gave them the bone marrow and was it just as effective?

Alison R. Walker, MD: So, for... Do you mean for the last abstract that I presented or for the...?

Q13: There would have to be a bone marrow transplant, one that you had up there that listed the people that have had chemotherapy and somebody had this 75 had nothing. Was that just as effective?

Alison R. Walker, MD: Yeah. So.... And again, this is... and I don't mean... because I'm not a transplant doc and it's not something that I do all the time and so... but there are some instances where a transplant doc will decide to take someone to transplant without giving them any treatment at all despite whatever is going on their marrow if they have higher risk disease and, again, it's interesting to me that those patients actually did just as well as the patients who had treatment whether that be with the Vidaza or Decitabine or intensive chemotherapy. So, I think it's probably a question more for the transplant community is as I was sort of putting this together and kind of thinking more about them. Do we need to treat patients before they go onto transplant or given that there's no additional benefits sort of in the long term and there may be some transplant specific things that I just don't know or there's a reason why you'd want to do something, but this data would suggest that you really didn't have to because there really was not a difference.

Q14: I've been on Aranesp now for 2 years and do you ever have the side effect of arthritis which I have never had before this in my arms and my leg.

Alison R. Walker, MD: So, did that start after you started the therapy and has gotten worse as you've been on it?

Q14: It has only started in the last month.

Alison R. Walker, MD: It's not something that I have commonly seen in my patients, but I also think that everybody is sort of individual in terms of how things... and that's always what makes

it hard in terms of is it something that's just affecting you or is it something sort of a general kind of things. Have you tried anything to help that, your symptoms or anything like that?

Q14: No, because I'm not even sure it's arthritis. I've never had it.

Alison R. Walker, MD: Again, it's not something that I've commonly seen or all of my patients mention that or have that as a symptom.

Q15: When you talk about the transplants, what hospitals locally are qualified to do transplants? I'm not sure not every hospital does that sort of thing.

Alison R. Walker, MD: Sure. Yeah you have to... and again I don't know all of the logistical sorts of things, but you have to be sort of accredited to do bone marrow transplants and so here in Columbus I believe the James and Ohio State is the only place, but there are institutions. I want to say Cincinnati Jewish and then, of course, Cleveland Clinic and those are the ones that come to mind, but they have to be officially kind of accredit... because there are all of these rules and regulations about quality measures and cell processing and there's all sorts of things that kind of go along with that which is a little bit different than sort of the requirements in terms of acute leukemia or MDS.

Q16: You mentioned that something about MDS after prostate cancer and this is the first... We've researched that and were told that there was no connection. Is there a connection?

Alison R. Walker, MD: So, I think that it's somewhat controversial. My personal opinion is that for patients that have received radiation or seed radiation particularly in the prostate which is, of course, in the lower pelvis which is where your bone marrow is I can't say that there isn't some influence of that treatment to bone marrow problems that develop later and so that's been my... not that there's nothing to do about it, but in my mind I think that it plays a role.

Q17: Are you familiar with the Deferoxamine to extract the iron?

Alison R. Walker, MD: Sure.

Q17: The side effects of it, the severe pain and what we can do to help with that?

Alison R. Walker, MD: So, tell me a little bit more. Is this that you're experiencing?

Q17: My husband.

Alison R. Walker, MD: How long have you been on the agent for?

Q18: For a year.

Alison R. Walker, MD: For a year and tell me a little bit about what it's been like for you.

Q18: In what manner?

Alison R. Walker, MD: What symptoms have you been having or what did you notice first and how long did it...

Q18: Severe pains.

Alison R. Walker, MD: Just pain. Just generalized pain.

Q18: Yeah. From my knees to the middle of my back.

Q17: (inaudible 51:06)

Q18: Yeah.

Alison R. Walker, MD: What did she say?

Q18: She said the groin.

Alison R. Walker, MD: The groin area.

Q18: That's where the major pain is from my knees to the middle of my back.

Alison R. Walker, MD: So is it constant pain or is it something as soon as you take...

Q18: It happens a couple three times a week.

Q17: Mainly at night.

Q18: Yeah. Mainly at night. Severe pain.

Alison R. Walker, MD: Actually, I have had some patients that have had joint pains and discomforts for short... severe pains like that, middle of the night waking them up is sort of what it sounds like to me. Patients haven't had. Certainly all of the nausea, vomiting, diarrhea. Those sorts of symptoms my patients have had but not severe pains like that, but, again, like we were talking about everybody is individual in terms of how things are going to respond... how they're going to respond to therapies. Does anything help at all?

Q18: Yeah. They put me on pain pills.

Alison R. Walker, MD: I wish I had... Gosh, I wish I had something to tell you that could fix that, but I don't. How long have you... and you said you been on it for a year?

Q18: Yeah. A year.

Alison R. Walker, MD: About a year. Okay. Do you have low risk or high risk MDS?

Q18: I have low risk.

Alison R. Walker, MD: Low risk MDS.

Q18: With high risk symptoms. I see Dr. Klisovic.

Alison R. Walker, MD: In patients like yourself, certainly there's a big benefit for doing iron chelation and so I wish there was something more I could recommend for that. How about an easier question?

Q18: Thank you.

Alison R. Walker, MD: You're welcome.

Q19: Is there a medicine that they're working on that you could take when you get a transplant now? It's fairly new I understand. The Cleveland Clinic and Freddie Hutchinson... I've been reading about it on the computer and I've been told about it a little bit is that do you know anything about that medicine?

Alison R. Walker, MD: Can you tell me a little bit more about what you read?

Q19: I may be a person that may have to take that transplant and they're working on a medicine at Freddie Hutchinson and Cleveland Clinic and I don't know what the other one is and it's in... if I take a transplant that medicine would be used and they're having pretty good luck with it. Do you know anything about that medicine?

Alison R. Walker, MD: So, there's a lot of different things that could be going on and in development at the individual centers and so it's hard... There's nothing that comes to mind. I think part of it is because I'm not a transplant doc. I might be out of the loop in terms of exactly what's going on in individual institutions and so I'm sorry I don't know exactly what agent you're talking about. Okay. An easier question.

Q20: I have a platelet question.

Alison R. Walker, MD: Sure.

Q20: I think... (Attendee) was diagnosed three years ago and his platelets, I think, when he was diagnosed they were like 125 and they, of course, fluctuate. His last blood draw a couple days ago they were down to 94. The lowest they've been has been 93. What's the low point when you'd have to start taking a treatment or getting platelets?

Q21: Transfusion.

Alison R. Walker, MD: Sure. My personal practice is when platelets fall to 15,000, we recommend prophylactic platelet transfusion. So, pretty far from where you are right now.

Q20: So, what (inaudible 54:57) for like if you (inaudible 55:00) eat a lot of kale, eat a lot of greens, eat a lot of broccoli.

Alison R. Walker, MD: I have a patient who with low risk AML and her platelets were sort of in the 100,000 range and she just started putting kale on everything like she would sauté bacon with it. I don't know you're supposed to be sautéing bacon with it all the time, but she would dry it and sprinkle it in soups and she really... she did that and then she did some other, I think some other multivitamin sorts of things and I don't have an explanation for it, but her platelet count did get better and kale is not bad for you. I don't have any scientific things that I can present about different foods, but I always recommend kale and greens to my patients just in the off chance that that might provide them some additional benefit.

Q19: And then a question about (inaudible 55:45). It seems like that's a common chromosome abnormality. Are they doing a lot of research on that?

Alison R. Walker, MD: So, the way that we usually look at chromosomal abnormalities which occur in about 40 percent of patients with MDS of one type or another is we look at what is associated with Trisomy 8. For example, patients with Trisomy 8 who are treated with X drug, do they do better, do they do worse, but in terms of something specifically about the Trisomy 8. So normally, people have two copies of chromosome eight and when you have Trisomy 8, you have three is there something about or within the proteins themselves or the chromosomes themselves that that having that extra copy seems to do. There's nothing that I'm aware of that suggests that, but we mostly look at once we get all this data from all these clinical trials then we sort of look at subgroups of patients and see how they do. So, it sort of depends on what treatment people are receiving. Trisomy 8 in general is considered sort of an intermediate risk, sort of chromosomal change.

Q19: It sounds like (inaudible 56:49) it's (inaudible 56:51) risk. In other places it's intermediate. So, you consider it intermediate.

Alison R. Walker, MD: I do.

Q19: And (attendee) also, he's kind of abnormal. I mean, I'm not been on any treatment for three years and he has a mutation, the ASXL1, which supposedly is a very progressive mutation, but it's not... thank God it's not doing that to (Attendee).

Alison R. Walker, MD: Yeah and I think that that's... and thank you for bringing that up because we're... it's an exciting time in MDS because we are discovering all these different mutations and we don't really necessarily know exactly what to do with them because we'll have patients like yourself that aren't following the book which always makes us scratch our head and say what are we missing and I think it's probably going to be another, gosh, five to 10 years before we can adequately look at this panel of... It's being done and a number of abstracts and presentations at the meeting this past December were about different groups looking at all those different mutations and oh, I found this new mutation and trying to figure them all out, but exactly how they relate to MDS, how they affect disease progressing, can they be modified at all with therapies. Those are things that we just don't have the answers to just yet.

Q21: Do you have any advice for spouses... I don't know whether it's not exactly caregiving at this point, but when the patient doesn't really want to know all the details, but you do and you've got a doctor that's not just giving a lot of information. What's a nice protocol to get the information that you want? What do you recommend?

Alison R. Walker, MD: So, a couple of things. One, having a conversation with your partner and deciding before appointment I'm going to ask this question. Is that going to bother you that I asked or if you want to leave the room while I ask or that sort of a thing just so sometimes as a physician, you don't want to impose or create strife in a relationship and under an already tense... you know, sometimes these meetings and discussions can be tense. I'll be honest for most of my patients who don't... Most of my patients ask me about survival or treatments and things like that, chances of relapse. Some people don't. For those that don't, I'll prompt and say, "I can tell you some numbers. Is that something you want to hear?" and if the patient says no, but the spouse says yes, then I'll say, "Well, is it okay if I speak with your spouse or partner separately?" and they say yes or no and then we kind of go from there and then sometimes what I'll do particularly if the patient is saying that they're not interested or don't want to know and I'll typically say something along the lines of and that whatever you want to do is fine. I'm curious, can you tell me a little bit what you're worried about or is there a specific concern that you have or belief or philosophy about hearing those sorts of numbers and for some patients it's they don't... it can feel like we're telling them what's going to happen, not everybody, but some people feel that way. Some people are people of faith and it doesn't matter what you say doctor. Whatever is going to be is going to be. It's not in your hands and which is fine and so I try to do my best to figure out where the reluctance is coming from and then I've had some interesting situations where sometimes the patient will then start talking about things that they felt uncomfortable talking about with their significant other and sometimes not. So, I wish I, again, had some more definitive, but that's how I personally approach it. Anything else? Sure.

Q22: When I was diagnosed three years ago, we were here in Columbus and I had to have three vials of blood drawn and all that. While that was being checked out, we went back to talked to the doctor and (Attendee) asked him what he thought it might be and he said, “MDS, but don’t look it up.” Of course, she went home and dived right into the Internet and found out a lot of nasty stuff and I was just kind of out there hanging out and not really involved with it. However knowing now that I have it, I found that it’s extremely interesting and I do want to know more about it. I even asked my doctor in Cleveland if I could go to the lab and he invited me up for two weeks.

Alison R. Walker, MD: Oh, that’s great.

Q22: I haven’t done it yet, but that’s a possibility.

Alison R. Walker, MD: Oh... And Dr. Tu (sp? 1:02:15) does so much work with those mutations. He and Dr. Maskiowsky (sp? 1:02:19) and Secarest (sp? 1:02:19) up there.

Q22: Right and what else... I lost my train of thought here.

Alison R. Walker, MD: I’m sorry. I didn’t mean to interrupt you.

Q23: I think sometimes knowledge is power. If you feel like it’s your time when you want to learn more about it, it will help you and I don’t know if some of you know Kirby Stone. He was very active in the world of MDS and survived, I think for eight years and he just recently passed, but his wife said that you need to take care of things you take care of and things that you out of your hands, don’t worry about it. Just take care of things right now that you can take care of and other things just...

Alison R. Walker, MD: Yeah and I couldn’t agree with you more. I think for each patient that happens at a different tempo and for some people it’s immediately when they hear their diagnosis and they’re meeting people and they’re joining support groups and they’re on the website and then for other patients it takes longer because I think that that’s just the normal variation and how you go through the grief of losing your good health. A lot of times this is a diagnosis out of the blue and then getting used to the terminology and the doctors and the blood draws and am I neutropenic and all of those sorts of things. I just think it happens. I’ve always been a bit of a late bloomer and just in general and so I feel like some patients it just happens for them at different speeds. It is really the job of your treating team to recognize that in you individually and kind of help you along. I want to make sure that I don’t get into your time. Any other questions for me?

Q24: When you were talking about Vidaza, you said that there’s generally there’s X number of cycles you go through and that there’re no results improvements that they discontinue it. What happens if they discontinue it after that? Where do you go from there?

Alison R. Walker, MD: I mean, it's a great question and if there's a clinical trial available... A little bit depends on what's going on. So for example if you were someone who was on Vidaza and had persistent transfusion requirements after that that hadn't improved and there wasn't a clinical trial then supportive care would be what I would recommend. I don't... My personal experience has not been one where people who receive Vidaza and then received Decitabine and then receive Lenalidomide. I think you have to use those drugs appropriately and sometimes the hardest thing as a doctor particularly at that point is to step back and say if I'm giving you more chemotherapy that's not going to work how is that benefiting you and what risk am I exposing you to? And so I think that it's harder to not do anything and that's especially if I don't think that it's going to give you any benefit or get your counts better or decrease your transfusion requirement just giving someone something just to give it in my opinion isn't the right thing to do unless it's going to have some benefit and there are instances and circumstances where you would consider those different transitions, but I really individually look at each patient that I'm caring for and we have a discussion about that and that's the hard part of MDS. That's the challenge that we don't have treatment after treatment after treatment to get to, but hopefully with these new agents that are coming that will change.

Q24: Another question. Between doctors...

Alison R. Walker, MD: And I know you.

Q24: ... and you can help me because I'll get it wrong, but we go to a hematologist and a dermatologist to try to control the skin things that go on because I have... and sometimes they conflict like what's good for my skin is not good for my blood and they do talk to each other. I'm aware there's conversations going on but is there a best practice between the hematologist and the dermatologist in term... because just recently we tried.

Q25: The drug is Dapsone he's talking about.

Q24: We tried some changes. Well, it just flared my skin by what he did and it's like I'd rather not do that again. My skin flares up. Yeah, it fixed the blood, but it flared my lesions and so how do you make sure that that the conversations that's happening over the fence is good for me?

Alison R. Walker, MD: So I think... and your story is a very unique situation in that you as I think... in my opinion I think part of your MDS... MDS can be associated with specific autoimmune sorts of diseases. Most commonly are things like hypothyroidism, but also it can have some things like Sweet's Syndrome, some specific sort of rash sorts of things, pemphigoid which is a type of rash essentially and it can be really challenging to figure out how to treat someone's MDS and also treat the skin problems. Sometimes we even consider treatment for the MDS as a way that sort of on the backend also treats the skin problems and so I think unfortunately for yours because I know that we've talked and there were just a lot of different things that were tried and flares and better and then the counts and things like that and so it's really just it's good that your hematologist and dermatologist are talking because that's going to

be the best way to figure that out and unfortunately sometimes it's going to be a little bit of trial and error and seeing can you get down a dose enough so that things sort of stabilize and then gets to some sort of equilibrium. It's going to be challenging. Your story, I remember, is very complicated.

Q24: I was wondering if there was some best practice. So, it's not common at all.

Alison R. Walker, MD: No, no, not common.

Q26: I have a suggestion. I have five or six specialists that I'm seeing and all of my specialists know that my hematologist... well actually, I have two hematologists. One in Cincinnati and one up here at OSU. All my specialists know that we do nothing without my hematologists' approval.

Q24: A lot of times I think we do that, but that's not what really happens sometimes.

Q25: And also sometimes our certain doctors once they find out about the MDS, they're hesitant to do anything with... I mean, first they say talk to your hematologist, but that's not his specialty and he says they should be treating you. Yes they can confer with me, but don't not do anything. Because we've had people not do anything just because I think they're frightened of the MDS of it affecting that part of it.

Alison R. Walker, MD: I think if your hematologist reassures them about that it's okay to do whatever, usually it usually works out okay. That's been my experience when I've had patients who've had just... because it comes up a lot because a lot of times if you have MDS, you have other medical problems as well that require some sort of treatment or surgery or a tooth pulled or this that or the other and sometimes it's just a quick call can help and it sounds like that's what's been going on though. Right?

Q24: It's frustrating a little bit because it's been a long time, but it still feels like we stumble over things like oh, well this did that and that's not good. So, we still find ourselves right there.

Alison R. Walker, MD: Anything else?

Q27: Talking about skin. During the winter time over the past number of years even prior to my diagnosis I had hypersensitivity to clothing and it will just... it's like prickly all over my arms and my legs and around my midsection and I wonder if that was related in any way to my MDS.

Alison R. Walker, MD: Not that I'm aware of. The skin changes specifically that are autoimmune sorts of skin things that can happen are actually things you can actually see like rashes and changes and things like that not so much skin. It's just general sensitivity.

Q27: One other question. I want to verify something I heard. I've heard that only five percent of MDS patients go onto have a bone marrow transplant. Is that correct?

Alison R. Walker, MD: Gosh. I don't know the number off the top of my head, but that number seems small to me. I don't know...

Q27: What percent of your patients have gone on?

Alison R. Walker, MD: So in my general practice, I would say... and part of this it's a little bit of selection bias because the patients that are referred to my clinic tend to be more towards the older range. I had more lower risk patients, patients who wouldn't necessarily require transplant because they, our schedulers, try to funnel those patients to Dr. Bloombetter (sp? 1:12:12) because of that patients... folks that see MDS and treat those patients and can take them to transplant if indicated or Dr. Vossi (sp? 1:12:18) So, I don't see as many. The ones that I do see, gosh, I would probably say... I would say a quarter of my patients. Yeah, I would and I pretty much refer... I refer all of my young patients, young being 65 or less to a transplant doc just for an initial evaluation and consultation just to get the information going just to kind of put that on the shelf in case things change more rapidly than anticipated.

Q27: We were proactive and we went on to a bone marrow transplant doc at Cleveland Clinic and he basically told me I don't want to... I hope I never see you again. That's what he told me.

Alison R. Walker, MD: Yeah and that's sort of the conversation that I want for my patients as well, but just to... I always think it's... sort of catching the eight ball or being behind the eight ball if things rapidly progress and I had a patient who is sort of lower-ish risk and then was high risk and AML in like eight months and so because we had sort of been more aggressive about getting that thing... all those things in line, we were able to kind of proceed relatively expeditiously towards transplant. He happened to have a sibling donor which made it a lot easier, who lived in Columbus, which made it a lot easier.

Q28: Is there any correlation between MDS and osteoporosis?

Alison R. Walker, MD: Not that I'm aware of. No. Other than the median age that people are diagnosed with, MDS is 71 – 70ish and so osteoporosis in and of itself is more common to older women, thin, Caucasian, those sorts of characteristics, but no correlation in the sense that MDS increases the rate of osteoporosis. Not that I'm aware of. That's a good question.

Alright. Great. Well, thanks so much for your time and attention. I enjoyed your questions. I wish you the best as you move forward with your docs and treating team. So, enjoy the rest of the morning.

Jean Ridgeway: ... get started. Remember I told you about the nickel I'm going to pass out to each of you. Most of us don't know each other. You certainly don't know me and in fact we just

go around the table and real quick just say your name and where you're from and I am geographically challenged. So, let me know if we're looking at Columbus as the epicenter if you live an hour north, three hours west that would be helpful to me just to kind of put you in place and give us the one thing you hope to get out of this meeting today. Okay? I'll start. So, my name is Jane Ridgeway and I'm a nurse practitioner. I work at the University of Chicago and I am an outpatient nurse practitioner. I spent many years as an inpatient nurse practitioner and I've been working with adult leukemia and stem cell transplant and probably half and half between malignant hematology, MDS, AML and transplant. So and I work in the outpatient setting and frantically finishing my doctoral degree. So, that's why I'm working in the back and am probably the most passionate about patient education and my one thing to get out of this today is to hear somebody say that they get it or they feel a little bit better connected. So, we'll start at the left with (Attendee).

Q29: I'm (Attendee).

Jean Ridgeway: You need to use a microphone thank you very much. Push the button.

Q29: I'm (Attendee) and I'm from Pittsburgh, Pennsylvania and I'm interested in what's next.

Q30: And I'm the wife, (Attendee) and I have the MDS and we just wanted to know more about it. We don't know what questions to ask.

Jean Ridgeway: How many people here have never been to one of these patient symposiums before? Who's the newbie? Alright. Who are the veterans? Ooo. Look at that. I'm impressed. Alright. Next. By the way, you get to keep your nickel because you were very good.

Q31: My name is (Attendee). I have MDS. I came to learn what's new. I'm down to the last thing and I live in Greenfield, Ohio which is about 60 – 70 miles southeast of here.

Jean Ridgeway: Thank you. (Attendee) is next.

Q32: I'm (Attendee). I'm here to find out if there are any new options on his MDS because I want to take the best care of him I possibly can.

Jean Ridgeway: Are you the wife, (Attendee)?

Q32: I am the wife. Yes.

Jean Ridgeway: Thank you for coming.

Q33: Hi. My name is (Attendee) and these are my folks, (Attendee) and (Attendee). I'm from Columbus and I'm just here to learn more about MDS and just best practices for treatment and make sure we leave no stone unturned as far as anything that could be new out there and so forth.

Jean Ridgeway: Very good. Next?

Q34: I'm (Attendee), patient for about three years. I'm here to learn as much as I can and not be confused by it. We live in Marion, Ohio, north of here about an hour.

Jean Ridgeway: Thank you.

Q35: I'm clumsy because I just (inaudible). Sorry. I'm (Attendee). I'm (Attendee)'s wife and we're here possibly to see if... meet some people that are live near us maybe we could start a support group and just learn more about MDS.

Jean Ridgeway: How many people here think that they're the only patient in their doctor's practice with the diagnosis of MDS? Anybody here fall into that category? A couple of people. That's a scary feeling. That's a great goal. I don't know honestly if the MDS Foundation can help share address. It's something that we can ask Dee and Audrey, but if you folks kind of... did you say (Attendee)?

Q35: Right. (Attendee). We live just an hour north of here (inaudible 1:20:43).

Jean Ridgeway: Well if any of you live around there think about that. Next.

Q36: I'm (Attendee). I was just diagnosed last summer. So, this is all kind of new learning the terminology and everything. So, I just want to learn more and learn more about the new treatments that are available.

Jean Ridgeway: And where are you from, (Attendee)?

Q36: Toledo. That's about two and a half hours northwest of here.

Jean Ridgeway: Thank you.

Q36: They're an hour. We're just another hour north. I'm (Attendee). She drug me out along and...

Jean Ridgeway: Did you leave your skid marks at the door? Was that what I saw from you out there?

Q36: Yeah and what I was hoping to get a little more information about that pill that you take once as the complete cure.

Jean Ridgeway: Oh, okay. Well, I'll keep our ears open for that. Maybe by the time we get way over here to (Attendee) we might have the answer.

Q37: Hi. I'm (Attendee). I'm from Cincinnati. I'm supporting my wife here and we come... I come just to stay informed and keep up to date with what's going on.

Q38: It is really confusing. You feel like you're learning hematology. It's something you never really wanted to learn and all of a sudden you're in hematology world and it's like wow, this is complicated.

Jean Ridgeway: It's very complicated.

Q38: I'm (Attendee). I'm from Cincinnati and we're here to be educated. We like to keep up to date.

Jean Ridgeway: Where is Cincinnati from here?

Q38: South. I'm sorry. South two hours.

Jean Ridgeway: Two hours south. Okay. Very good.

Q39: Hi. We're (Attendee) and (Attendee). We're from Pittsburgh, Pennsylvania. This is all new to us. I mean, the practice that we deal with was just very limited. We're just trying to get new information to see where we go from here.

Jean Ridgeway: The MDS does offer a list of "MDS Centers of Excellence" across the country if you're looking for a second opinion because remember medicine is a consumer driven business. The doctors are your employees. If you don't like what you're hearing or you want to get a second opinion and see if somebody's got something better to offer, I encourage you to definitely get a second opinion. If your provider is intimidated by a second opinion, you should run to the second opinion. So, that's very true. Well, welcome. We hope we can help fill in some of the blanks.

Q40: I'm (Attendee). I'm the patient. We're from Dayton, about an hour west of here. I just want to find out how to live with it.

Jean Ridgeway: And how long have you been diagnosed with this?

Q40: Three years.

Jean Ridgeway: Three years.

Q40: I'm on a wait and watch.

Jean Ridgeway: You're on the wait and watch. Okay.

Q40: So, I don't even take aspirin, but I know one day I will.

Jean Ridgeway: That's a cardiologist drug. That aspirin.

Q41: I am (Attendee) and I'm his wife and just here mainly to find out what might be new.

Jean Ridgeway: Welcome.

Q42: I'm (Attendee) from Columbus. Basically, here just to learn more and I guess hear some of the stories of other people that might be in similar situations. I'm a caregiver.

Jean Ridgeway: Okay. Welcome. Big job that caregiver job. Probably harder to be a caregiver almost in some respects than to be the patient as you feel so very powerless, I would say.

Q43: And I'm (Attendee). I'm the patient. If you want to trade, I'll trade.

Jean Ridgeway: That was not the best thing to say, but I think it's a really hard job.

Q43: It is a hard job, believe me because it's happening to me though, but anyway it's been... I was just diagnosed last year, only been a year, 15 months. So, it's all sort of new. I'm sort of in that mode of like if I ignore it maybe it'll go away and but we're happy to be here.

Jean Ridgeway: You're from Columbus also?

Q43: We're from Columbus.

Jean Ridgeway: I know where that is. Who's next down there?

Q44: Name's (Attendee). I'm from Newark which is 45 minutes away east. I've had the disease for four years.

Jean Ridgeway: And what do you hope to get out of it? Just kind of...?

Q44: Oh, just whatever like something's new.

Jean Ridgeway: Alright. Very good. Who's to the right of you? That person got skipped.

Q44: My mom.

Jean Ridgeway: Hi, mom. Moms are always there.

Q45: I'm (Attendee). I'm his wife and his caregiver and that's about it.

Jean Ridgeway: And you're from...?

Q45: Newark.

Jean Ridgeway: Newark and what do you hope to get out of it?

Q45: (inaudible 1:25:37) new information. I always enjoy talking to the other folks as well and I came to a forum last year and met some really nice people and stayed in touch with them through Facebook and that kind of thing. We talked about how to stay in touch with folks and it's something we had (inaudible 1:25:55) switched names through Facebook and got in touch with them and for the lady down here who was talking about the wife wanting... the spouse wanting to know everything, but the husband not wanting to know anything. Yeah. That's us.

Jean Ridgeway: That exists. Everyone, there're a million different stories and a million different circumstances and you live your own story.

Q46: I'm (Attendee) and I'm the daughter of (Attendee) and (Attendee) over here and I just came to show some support for them.

Jean Ridgeway: Thanks for coming.

Q47: I'm (Attendee). We're from Cincinnati. My wife was diagnosed a little over a year ago.

Jean Ridgeway: Christmas 2013 or Christmas 2012?

Q48: 2013.

Jean Ridgeway: 2013. Five months ago.

Q47: I'm just here to find out as much as we can about different treatments and support.

Jean Ridgeway: Okay.

Q47: I'm (Attendee). I'm the patient and as my husband just said, I just found out that I had MDS. I also found out a couple weeks later that I have a secondary bone marrow disease cancer called myelofibrosis. Even though I just recently learned that I have MDS, I'm already in chemotherapy for it and I'm already seeing a doctor up at OSU and we've started the process of looking for a donor for me and on Wednesday or Thursday I found out that my baby sister is a perfect match.

Jean Ridgeway: Congratulations.

Q49: Hi. I'm (Attendee). I've had... I was diagnosed in 2002. Other than taking the Aranesp shot, I hadn't... nothing else has been done. Keep losing my track of thought. I don't know information about this because my doctor has not told me a whole lot, but then I never asked him any questions, but I do have seven already written down. I'm from Elyria, by the way.

Jean Ridgeway: Where's that?

Q49: Elyria. That's 10 miles from Cleveland.

Jean Ridgeway: What a lovely name of a town. Next.

Q50: I'm (Attendee), the husband. I'm here because I don't know anything.

Jean Ridgeway: You're in the right place.

Q50: Yup. So, I wanted to get some steps to know how to move forward on some things and just back her up.

Jean Ridgeway: Perfect. Thanks for coming.

Q51: Hi. I'm (Attendee) and I'm the wife of (Attendee), the patient, and this is all very new to us also. So, I'm here to learn and I wanted to experience a forum in person. I listened to some of the recordings on the MDS Foundation site. So, it's good to hear.

Jean Ridgeway: Thank you for coming. (Attendee). My twin brother's name is (Attendee), which is why I'm going to remember his name.

Q52: I'm (Attendee). I'm the patient as my wife said. It's about eight months into since my diagnosis. I just finished my second cycle of Vidaza yesterday. So, I'm from Cincinnati also. We live in the same house actually.

Jean Ridgeway: Thanks for clearing that up.

Q52: I'm just here to find out what's going on, try to get some more information about the whole MDS thing and what you can do, can't do, what's good, what people... what other people are doing, that sort of thing.

Jean Ridgeway: That's good.

Q53: I'm (Attendee) and my husband was out playing tennis this morning and trying to just live life. So, I wanted to come and meet people and interact and just see what's going on with others. His counts were low for quite a long time and so five, six, seven years ago it was on the radar screen, but the official diagnosis was about three years ago. He's in his... I think we start

tomorrow or Monday, maybe the thirtieth cycle of Vidaza. So, it has worked for him really well. Dr. Bloom who we saw recently said it's kind of like a remission, so enjoy it while you can. We did do a little homework for an eventual transplant and a perfect "there were multiple matches," but a perfect donor, we have no idea or where, but that's in the background because at 29 months we kind of keep wondering when the other shoe's dropping, but so far so good.

Jean Ridgeway: Very good.

Q53: And I'm from Columbus.

Jean Ridgeway: And you live in Columbus.

Q53: Worthington.

Jean Ridgeway: Okay. Very good. Well before we go any further, let me just pitch something to you all in case you haven't seen it, don't have it. This is something that you need to either go home with or get on the Internet and get a PDF file or ask the Foundation to mail you. This is an actual one. I just picked it off the table. I think this is probably not because I'm biased, but it really is true. I think this is the best source that you can go to for Myelodysplastic Syndrome. This is a very comprehensive book that was put together by lots of folks. I've written some of it. I've been... I know a lot of the people have written other parts of it, but the best thing about this is that it's geared for patients and for caregivers. So when you open this type of information, it starts at the very beginning. It assumes that you know nothing and builds from there. So, I would encourage you if you don't have one, here's one... I don't know if there's anybody who doesn't have one who wants to go with one. Here's another one. I'll just leave it up here. You can feel free to take it, but I think this is probably the best place to start and if you visited or haven't visited the website for the MDS Foundation that is another excellent source. It has prerecorded sessions like this as well as lots and lots of other information. So, I would definitely say that you're missing something if you don't get a copy of this and they're glad to mail them to you and they're free and so I think that's a great place to start because more than anything you want your information to be correct. I think there's a lot of myths out there. There's urban mythology. There's people who are well intentioned. I've heard some of you talk around the room that physicians aren't really open about telling you. Don't read what's on the Internet. There's not a lot of information and so I think we live now in an era of information. The information highway and people want information. It empowers us and that's a great place to go. So, like I told you, I like to stick to time. So, we have 15 minutes and what we're going to do is these are slides that look at this book and a lot of the information in it. So, it talks about like what is MDS, how to live with it, etc. So hopefully as we kind of go through this content and a little more simplistic fashion than the physician did with you, we can answer some... I can answer some questions for you. This isn't a classroom, but you know what? If you want to stop, just put your hand up so I know that you want to ask a question. We can go through questions all the way through. So, we meet here until noon. We'll break for lunch until one. We'll come back from one to two and finish. Okay? And we'll finish at two o'clock. Alright? Very good. Okay. Off we go.

So, the name of this resource really is called *The Building Blocks of Hope* and I'm going to tell you that when I went to nursing school, I went to a very reputable undergraduate nursing school, but I have... and I just don't remember a thing about hematology. I'm sure we learned a little bit about it, but I didn't know much about it and I started my career at the University of Illinois. It's in Chicago and I worked on a floor with hematology and oncology patients. So at that point in time, everything was kind of blended together and if you wanted oncology care, you went to a big academic medical center. People knew about Mayo Clinic. People knew about Cleveland Clinic, but it really wasn't out into the community and now we look at very highly trained physicians out in the community. So, we don't have to travel too far for care which is good because if you can get identical care at your local physician, it doesn't make sense to travel really a great distance. Now, sometimes that's not true. If you enroll in a clinical trial, you may have to travel to OSU or to the National Institute of Health in Bethesda depending on where that trial is offered, but all in all we've come a long way and there's a lot of good information out there and as I started my career as a young nurse, one of my parent's friends showed up on the floor and he had MDS, but they used to call it preleukemia and I was absolutely dumbfounded. I'd never heard about it ever and that's really where I became very interested in what was going on in the world of malignant hematology and have made it my passion to help my colleagues in nursing to understand what this disease is all about so that nurses can give the right information to patients. Right. Because you spend a lot of time with the nurses. Correct? I mean if you're not in a watch and wait situation, if you're in infusion therapy, you're interacting with the nurses a lot and you're asking a lot of questions and we need to give right information and then also like how do you figure this out? Somebody said they felt like they're learning a new language or they've entered a new culture. You absolutely entered a new language and a new culture. So, you're starting at the beginning and so I'm hopeful that some of this information will be absorbed and translated into some things that you can take home.

So, what's covered in this presentation, we talk a lot about understanding the diagnosis of it, what is it, what are my options? You talked a little about that. What are some of the treatments? What's new? What happens if I get a lot of transfusions? It sounds like the gentleman down at the end was talking about Desferal or Deferoxamine. If you have lots of blood transfusions what can happen is you can get a lot of iron and iron is not excreted out of our bodies. We just continue to build it up and it can build up in our organs and so it's good to somehow get rid of it, but sometimes the therapies to help the problem can be more problems than the therapy. Get aches and pains. Some people get diarrhea from those agents. They're not so easy to take. So, it becomes a real balancing act for you and your caregivers and then we talk about transplant a little bit and then what can I do to keep myself healthy. So, I'm going to put one pitch in here. The best... One of the best and kind of easiest things that you and your family and caregiver can do to stay healthy is get a flu shot when they come out in the fall. If you didn't get yours already, we're kind of like now past the end of flu season. Thirty thousand people a year in the United States will die of influenza. So, if you... As a patient who has MDS, you're just more vulnerable. Your immune system is not very intact. Even if you have pretty robust blood counts, you're immunocompromised. So, you need to cocoon yourself as best as you can. So, get that flu shot

and everybody else in your house needs to get it too. Okay. Don't get the shot for herpes. Don't get that one unless you have okay blood counts because it's a live virus and you could develop disaster. So the flu vaccine is a dead virus. It's very effective, but the herpes shot is a live virus. So, you have to be careful with that. So, that's just kind of like one little pitch. Now, I'll go back to this stuff.

Okay. So, we talked a little bit about *The Building Blocks of Hope* and there's lots of stuff in there and it was created out of a movement of people like yourself. As MDS first became diagnosed and recognized as a standalone diagnoses, a group of folks who like were given that diagnosis got together and formed this organization so that they could become better educated, their caregivers and their families could become better educated and all of this fits into those goals that the organization was put together for.

So, let's talk about MDS. What is it? Aren't those pretty little pictures up there? You know what that is? That one to my... So, looking up here to the right. That's your bone marrow aspirate. When you get a bone marrow aspiration and they take that liquid out and they put the material on the slides and they stain it, when the pathologist begins to look at that and analyze it for components. Are they normal? Are they abnormal? What's there red cells, white cells? Are there any of the naughty blast cells in there. That's what they're looking at and those very large cells that kind of have the big purple circle in the center, those are blast cells. So, blast cells... Give you a little pathology update. When we do a bone marrow biopsy with you, why do we do that? You know, why can't we just look at your blood counts? We do that because there's really... there is not a parallel between what's in your bone marrow and what's out in your blood. We've seen patients who have totally normal blood counts and have a very dysplastic bone marrow. So, what are they looking for? They're looking for a few different things. They're looking for a number of blast cells. So, what's the percentage of blast cells? So when blood cells form in our bone marrow, everybody comes from a mother cell. Like the mother ship. So, that's called a stem cell and when you get a stem cell transplant, what you're really getting is a high concentration volume of somebody else's stem cells. Now, those stem cells are really unique because they do one of two things. They either self replicate which allows us to continue to have them or through a series of hormonal influences and other messages from your bodies, they become either one family or the other. So, there's two major families in hematology. One of them is called the lymphoid family and the other one is called the myeloid family and the myeloid family cells when they're all grown up and they're productive members of blood society they do one of three things. They become a red blood cell, they become a white blood cell or they become a platelet. So, that's where the grownups should be and that's what you should look like when you grow up. However, what happens with Myelodysplastic Syndrome is that somewhere between first creation I'm going to be a myeloid cell to the terminal differentiation or what do I look like at the end, something happens along there and there's an error. Some cells stop in growing up and they just mature out to this very, very immature cell and it's called a blast. So normally, the blast cells go ahead and grow up into normal cells, but when they get stuck in immaturity, they're called a blast cell. It's normal to have a few in your bone marrow, up to five percent. If you have more than five percent then you've been tipped over into a disease

state because that's normal to have more than five in your bone marrow. So, they look for blast cells.

They also look for something called cellularity. So, what's that? So, cellularity when you read your bone marrow report and if you haven't gotten one you should get it because it's your information. It'll talk about cellularity. That's always a ratio. It's a ratio of how much tissue of your bone marrow is producing cells versus how much fat do you have in your bone marrow. So, the bad news is the older we get the fatter our bone marrow gets, which means the lower cellularity we get as we age and it's always an equation. So, it's 100 minus your age should give you what your cellularity. So, I'll give you an example. So, if I'm a 50 year old female and I have a bone marrow biopsy and I read the cellularity and it says 20 percent cellular. That's too low. Correct? Because if you took 100 minus 50 because my math skills are okay, it should be 50 percent, but now I'm 20 percent. So, that says that I'm hypocellular. That's easy. Hypo always means too low. So, I'll take the same situation and I get my bone marrow report and it says that I have 90 percent cellularity and that's too high. Right? So, that says that I'm hypercellular and what do those things mean? If you're hypocellular, chances are that your counts may be a little bit lower. Maybe you have an infection. Maybe you're taking some medications that can depress your bone marrow. There's some medicines that can do that. What does it mean if you're hypercellular? Hypercellularity usually means that your bone marrow is really, really active and so if I had the unfortunate event of having a bad car accident and I bled all over the place and they were trying to figure out my anemia and they did a bone marrow then I might have a hypercellular bone marrow, but the other reason usually is that it's trying to keep up with something like an MDS or even with acute myeloid leukemia. So, cells get very, very active and they mature, they mature and they're in that bone marrow, but you may be somebody who has a hyper cellular bone marrow, but you have low blood counts and how does that happen? So cells just don't get out into the periphery or they're stuck in that immature phase and you have lower counts. So, those cells just don't grow up. They stay babies and that's not a good thing. So, that's what cellularity is.

And then they also look at your cytogenetics and I heard the physician telling you a little bit about they want to see the DNA of the blood that they're pulling out of the aspirate and that's absolutely true. So, it's not constitutional DNA. Constitutional DNA is the stuff that you see on TV when they say who's the baby's daddy. That's what constitutional DNA is, but for MDS it's does the disease have some certain characteristics? Trisomy 8 I heard somebody over here talking about. Does it have a deletion 5, 5Q or some other? There's lots of them out there and that's what they're really looking at.

So, what do we know about Myelodysplastic Syndrome? So, it's evolved in its nomenclature from preleukemia, smoldering leukemia and now it's definitely got a name called Myelodysplastic Syndrome and that means that stem cells produces either a myeloid or lymphoid. So now, you know that the M in Myeloid has to do with that family and just like in my family if somebody misbehaves it affects the rest of the family. So if your red blood cells are misbehaving, it's also having an influence on your white cells and your platelets as well. So,

that's the M in Myelodysplastic Syndrome and we know that it's a group of bone marrow cancers and it is a malignancy so we do call it a cancer. There's a little bit of grey zone out there when you go to your various practices. Some people say it's a cancer, some people say no it's not a cancer. So from the MDS Foundation and even from the World Health Organization, MDSs are considered a blood cancer. Now, Myelofibrosis is another bone marrow disease that kind of intersects with MDS like if you saw concentric circles and there'd be a lap over. Sometimes Myelofibrosis which is a myeloproliferative disorder overlaps with MDS and sometimes people have both concurrent problems going on at the same time, but there are a whole spectrum of disorders. There are people I heard saying watch and wait. Some people are getting Aranesp only, 30 cycles of 5-Azacitidine. So, there's a lot of variability both in what type is it and how is it going to behave, but it's a whole heterogeneous group, all different types of groups of diseases and we know that it's a stem cell malignancy. So, the malignancy in the error is going to happen in the mother ship. So, it happens in the stem cell. That's where it's originating, but it may not show until a little bit later and, again, it's not just one disease, but it's a lot of different ones. Things look different. The disease can behave different and because of that there's a lot of different suggestions from your physicians on how you treat this disorder because what's good for me is not going to be what's good for John, but if you sit down in the doctor's office and you're kind of sharing with someone, I would caution you to just keep that in mind. This is not a disorder that behaves identical in every person. If anything, I would say uniformly it behaves different in everybody, but there's a lot of commonalities within it.

I think it's twelve o'clock. Dee has come in to tell us that there's lunch. So, with six... we have six minutes? Who's got the right time? Okay. Six minutes.

?: (inaudible 1:47:53)

Jean Ridgeway: Yes, ma'am.

Dee: If anyone wants another copy of *The Building Blocks of Hope*, we have two. You want one. Okay. Good. Anyone else? We have (inaudible 1:48:04). Anybody else you can share it with your children, relatives. You want one? Okay.

Jean Ridgeway: Really have three because here's another one.

Dee: Oh, yeah. That's (inaudible 1:48:16)

Jean Ridgeway: I can't fit this in my carryon. Then it won't stuff into the overhead baggage. Alright. So is everyone... Does that make sense to people what kind of questions...? What kind of questions do you have about that as a kind of an opening venue to MDS? Make more sense? Doesn't make more sense? Does it make more sense? Okay. How many people in here have never had a bone marrow biopsy? Come on caregivers, raise your hand, you babies. Okay. So unfortunately with this disease I will tell you you must have a bone marrow examination to make the disease. Absolutely. That is... Uh, oh. Hand up.

Q54: Do you have to get them subsequently...

Jean Ridgeway: Yes, you do.

Q54: ... and how often?

Jean Ridgeway: So, the question is do you have to get them again? People around the table who have had one, you have to get one again? Yes, you do. What's the frequency? Depends on your disease. Depends on your disease. So, they're not the worst thing in the world. They're not the best thing in the world. You disagree. The couple I've had they haven't been so bad and I will tell you I do about 500 of them a year. So, I do quite a few of them on folks. The more you do the better you get, so but don't get a fellow. That's what you don't want. Anyway... But you do. You absolutely have to have one to make the diagnosis because why? We talked about that what you use in the blood and what you see in the bone marrow do not parallel one another. So, you really have to look and they've got to also look at... They look at something called the architecture of your bone. So, the core biopsy piece it's sliced up and then gets looked at and they truly look at what does the tissue of your bone look like. So, somebody over here mentioned about prostate cancer. Right? So when men have prostate cancer and if they've had radiation for prostate cancer, where men get radiated is if you could draw a little rectangle all and cover my pelvis and then cover the back of my pelvis, that's where the radiation happens. So, we know that unfortunately some men who survive radiation after their prostate cancer can develop a secondary MDS or even an acute leukemia because of the exposure to the majority of stem cells that are going to create your bone marrow. So, there is unfortunately a low... It is a low incidence of therapy related MDS, but it can happen. It can also happen if you're a woman who's survived breast cancer and you've had chemotherapy. There's another one. Our largest group of cancer survivors are folks who have survived Hodgkin's disease. You've heard about that Hodgkin's lymphoma? That's kind of a usually a younger person's disorder and it's curable, but they get very high doses of chemotherapy in bursts like every other week bursts for about six months and these folks are showing up now they've survived as young people and as they get to be 50 are showing up with secondary malignancies and it's unfortunate, but they've survived their initial... they've survived their initial cancer and so now they have this secondary one because why? Because that stem cell got injured and it did okay for a number of decades, but unfortunately as we age our bodies just don't recover like they used to and actually our DNA repairs itself all the time, all the time, all the time, but we can lose the ability to correctly create new DNA. So and then we begin to see issues with malignancies and some other... even health problems. So, alright. So, that's MDS. Not one disease. Right? Alright.

So again, they look at these cells and what they're looking for when they see the cells is that they don't look normal. They're dysplastic and that's the fancy word for saying an irregular shape. So if I was a fully trained hematopathologist, which I am not, but I do spend some time down there looking at slides, I could look at a slide and say that this one's normal and this one is abnormal and so part of the expertise in getting a diagnosis in MDS is having your slides evaluated by a

center that really specializes in malignant hematology. Mayo Clinic used to be very famous, but now there's lots of good hematologists and pathologist can look at it but the cells are dysplastic. So, dysplastic cells are like putting square wheels on your car. So, you got some wheels on your car, but when you go to pull away from the curb, are the wheels going to work as well as the round ones? No. So what happens when cells don't have the shape that they need, they can't perform the function that they were designed to do. So, the dysplasia plays right into that and then you have something called ineffective hematopoiesis. That's a fancy-shmancy way of saying that like you just don't produce blood cells like you should. Is hematopoiesis. Hemata is blood and poiesis is growth. So, you just don't have normal growth and development of the blood cells that you need. So, what you really need to live well are normal red cells. Right? That's reflected in your hemoglobin or your hematocrit whichever your practitioner follows. You need to have normal white blood cells and you have normal platelets and I will say that some folks can have kind of a normal white count. Normal white cell count is 3 ½ to 11 ½. That's the normal range, but these folks are going to be more prone to infection because the cells aren't shaped correctly. So, they're not going to have their full functional power because they just don't... they're not the right shape and they're not going to be able to perform that function. The same with platelets. People can really have a lot of difficulty with bleeding. Now, there are other ways your body can step up to help manage that, but it does happen. So, what else happens? So then, you have these cytopenia. So when you're down in any of those three cell lines. So in MDS, you're always are talking about the red cells, the white cells and the platelets. Correct? If your red cells are down they say you have anemia. Correct? Right. How many people in this room have gotten a blood transfusion? A couple. Just a couple. So, that's what can do to help people who have low red blood cells. Other people can get a drug called Aranesp or Darbepoetin. That's a red blood cell stimulator and it will work if you need your red cells stimulated and it's a hormone that's usually excreted by a gland that sits on top of your kidneys and most of the time practitioners use it for people who have a lower risk MDS and it can work for about a year usually and then the more hormone you give somebody if the problem isn't deficiency in hormone it's like pouring water into a full glass. You just don't need any more. It's not going to make any difference. So, how about if you have low platelets? That's called thrombocytopenia. What can we do if people have startlingly low platelets? We give them a transfusion. At our institution, I'll tell you we don't use 15. We use 10 or even lower. So, it just all depends on when you transfuse. It depends also on people's risk of bleeding. So if you're somebody who has a propensity to have some bleeding in your eye then we would keep it a little bit higher. So and a platelet transfusion can be given as an outpatient. Correct? And a red blood cell transfusion, same thing. The new guidelines from the American Society of Hematology is transfusions at 7 grams per deciliter and that's pretty low. A lot of people will... a number of my patients come in maybe weekly or every other weekly or twice weekly, but they'll call and say, "I need a transfusion." Let me check my CBC and sure enough they're right because how do you feel when your red cells are low? Tired. Right? You're more tired than you are normally and it can help you feel better. Usually, you have more of a kind of that like uplifting benefit when you first start with transfusions, but as you go on with them you lose that kind of like up feeling, but your body does work better with oxygen. So even though you don't "feel better," your heart says thank you, your kidneys says thank you, your brain says thank you. You can think better. So

everything works better with a little oxygen and that's why you want to make sure that your red cells are up. Question?

Q55: Since you're on this particular subject, (Attendee) was diagnosed 17 years ago with thrombocytopenia.

Jean Ridgeway: Thrombocytopenia.

Q55: (inaudible 1:57:13)

Jean Ridgeway: Platelets are low.

Q55: Was almost nothing and she was bleeding everywhere and blah, blah, blah, blah, blah. They put her on high doses of Prednisone and something else. I don't remember. Anyway. It all ended up and it was idiopathic.

Jean Ridgeway: That means they don't know why it happened.

Q55: Exactly, but we never really consulted a nurse practitioner about that who I happen to think in most cases are smarter than the doctors. No, I really believe that because I've dealt with a nurse practitioner and it was wonderful, but anyway our hematologists now is telling us that she's been diagnosed with the MDS affecting her red cells. There's no connection whatsoever.

Jean Ridgeway: I would say that that's true. There's a phenomenon called idiopathic thrombocytopenia or ITP and it's a very common phenomenon. It only affects the platelets and it tends to be an autoimmune self-limiting problem. It's really common in kids and it can be really common if you get a bad viral illness. So say you get a bad viral pneumonia and you're otherwise healthy, but you're like oh, my gosh. I'm bruising all over the place. What's going on? If you go to the doctor and they see that you just have low platelets they'll look at the platelets and a couple other lab values and they treat you with high doses of Prednisone probably over a four week period to get you off and then they monitor that blood count and usually it resolves. It's idiopathic. They have no idea why it happened and they know if they can fool your immune system enough to reset the clock basically to normal, it'll be normal and then never happen again.

Q55: Okay. So now that you verified that, we'll believe our hematologist.

Jean Ridgeway: That's good. But it's true and kids get it all the time and in kids it can be more severe. Sometimes little kids have to get their spleens taken out.

Q55: That's what our family doctor told us is that he's seen in kids all the time, but in an adult it was a little bit unusual.

Jean Ridgeway: It is unusual but it's not... never... it's not that it never happens. So, it's good that it's self-limiting because that other... she presented that one slide about aplastic anemia which is another bone marrow disorder and those people have terrible problems with their platelets.

So anyway. Last thing on the slide then we'll go to lunch. What about the risk for developing leukemia? So here's another secret of hematology. When all the people who created these nomenclatures for diseases and how you can call an apple and apple and an orange an orange. In the world of hematology that blast cell count is everything. So, the World Health Organization revised their standards and we'll look at it a little bit more, but basically now if you have from 5.1 up to 19.9 percent blasts in your bone marrow, up to 20 percent blasts in the bone marrow, we still call you MDS. When you take the imaginary step over 20 into 20.5 up to 100 percent, we now call you acute leukemia. Now, there's some other variability in there. Way too complicated, but that's the bottom line. So when you talk about is there a risk of developing leukemia or transforming into leukemia, the answer is yes. Maybe 10 to 15 percent of our patients who have MDS do transform. If you think about it, if you're somebody who has low risk MDS then you probably have a small percentage of blasts in your bone marrow, maybe a four, maybe a five, maybe a six. So the difference between six and 20 is pretty large, but if you're somebody who gets diagnosed and you have 18 percent blasts in your bone marrow. The difference between 18 and 20 is rather small and with that initial diagnosis what intuitively you think about is how long is it going to take that person to cross over in 21 percent? So if you think about it, folks who are watch and wait, just have anemia, they have a low risk and so they're probably not going to transform into acute leukemia but when people get diagnosed and they're a little bit sicker and they have a higher percentage of blasts, they're that much closer to acute leukemia. So, there is the risk and that is the natural history of this disease is that it can transform, but very few people do transform into acute leukemia.

Alright. Time for lunch.

Dee: (inaudible 2:01:42). We have a survey. So, I'm going to give it to you right when you come from lunch. (Inaudible 2:01:52)

Jean Ridgeway: Yeah. If you just kind of like fill them out when you get bored then you just like color in the circles or you write smiley faces, whatever you'd like. So, enjoy your lunch. We'll come back in here. We will start promptly at one o'clock your time. I'll reset my watch. I'm running a little early.

Dee: Thank you.

Jean Ridgeway: They got some jackhammers across the street fixing the parking lot structure. So, that should be fun. Don't fall asleep because we'll all make fun of you. You only have an hour. So, we'll go from there.

So now, back to a little bit of biology for understanding and then I want to be prompt and leave time to for sure for questions.

So, here's a great picture. This is from the National Institute of Health from their website and what we're going to do is so here's your bone. It's a femur. Maybe humerus, whatever. So, there's that stem cell that we talked about, the mother ship. So, there's a hemopoietic stem cell and then there's this other thing multi-blah, blah, blah, but that's okay. You don't have to worry about that so much, but look at there's the myeloid progenitor cell. That's a fancy way of saying I'm a member of the M family. I'm the next leader and that's what I should grow up to be when I'm a normal... If I'm a normal healthy functioning adult if I'm a myeloid cell and then there's that lympho... The lymphoid cell, that's the L family. If you know anybody who has a disease called multiple myeloma, which is totally different than MDS, those people have a problem in the lymphoid cells. So, it's totally different, but it's in the book and it's... So, that's good.

So what happens with Myelodysplastic? Where is the defect and how does it affect it? So, biologically this is what it looks like when it's normal. So, what's going to happen in abnormality and in MDS is that there're all these different factors that cause the bone marrow cell and the stem cell to produce. We talked about the immature cell, the blast cell. Correct? So, there they are and you're going to have lots and lots of immortalized immature blast cells. So, I forgot to tell you something that's really interesting in cancer is that the cells lose their ability to die. So normally what happens is cells grow up, they lead their useful life and then they're replaced, but in cancer, all types of cancer, the cells lose that death process and they become immortalized. So if you begin to think... Is anybody in here in accounting or banking or like does money or number things. Anybody in here like numbers? Well, I'll pretend. So if I said, "Would you rather have a penny a day for a month and I'll double it every day or would you rather have a \$1 million?" How many people are going to want \$1 million? A million dollars? Okay. How many people want the penny a day and double it at the end. You're the smart ones because by the end of the month you're going to have about \$3 1/2 million because one is two is four is 16 is 64, on and on and on and that's what happens. So if one little cell escapes the immune surveillance, escapes the police then they begin to multiply. Now, that process may take years. It may take decades and the thing thinking is that perhaps one of the reasons we see MDS as a disease that affects most people later in life is that this process happens undetected and it takes a long time for those cells to build up and so as they build up what they're going to do is they're going to crowd out all the other normal cells. Right? So in this diagram what they're trying to tell you is now you have all these blast cells and so this process is really very much deferred. So I told you that what happens in your family always affects the rest of the family. So if you have a 16 year old daughter who has a fit and goes into the bedroom and slams the door, it definitely affects the rest of the party. Right? So when your MDS cells behave very badly and they begin to grow like that, they're going to crowd out and push out the normal hematopoiesis and then what you begin to see then is that the peripheral cytopenias, that's a fancy way of saying your blood cells, then everything begins to drop. Now, you know that for some people they have anemia only. So, MDS looks lots of different ways. You can have those three cell lines. You can have one cell line down. You can have two cell line down or you can have all

three. So, it looks a lot different and again to diagnose it, you got to have a bone marrow biopsy and they do lots of other tests. We talked about the cellularity, the bone marrow blasts. Other things that they test though are iron saturation and they test some vitamin levels because some vitamins are the building blocks of red cells. So, B12 is an important vitamin. Iron is important, but if you get blood transfusions, you're getting non-excretable iron. Folate is another one. People oftentimes with B12 deficiency, those are the people who drink their lunch instead of eating their lunch. So, sometimes we have people who come in who may have an anemia and they have funny looking cells and sometimes the problem is too much alcohol. Now, stopping drinking of alcohol won't cure your MDS, but if you don't have MDS certainly that can cause it. There are medicines sometimes as people are trying to figure out the diagnosis of MDS that can trigger it as well. You should have your thyroid tested, your testosterone level tested and then they look at your kidneys and then your liver function as well.

This is a busy, busy slide and what it says across the top there's a bunch of initials. So, these are the classification systems. So, remember I told you that back in the '70s it's when MDS first got its own diagnosis and that's because the French, the American and the British pathologists said that we all need to speak the same language. So that as I describe a cell to my French colleague they can call it the same thing. So, it's called the FAB after French, American and British and if you have a bone marrow report you may have either an FAB classification or a WHO classification. So, WHO it builds on the FAB, but it also builds lots of other components that now are common in testing for this disease. So when you look at FAB, the big thing is it says a couple things. There are five categories, four of the five have anemia in them. So, what does that tell you? It says... It tells you that most people with MDS have a problem with anemia. As a matter of fact, 85 percent of all people with MDS have anemia. So, it's a big player. Red cells are greatly affected and these, RA means refractory anemia. RAEB means excess blasts and now you know that means that's more than five percent and there are different categories. Excess blasts in transformation and then there's this subcategory called CMML, chronic myelo monocytic leukemia which now has been pushed over into that myelofibrosis MPD, myeloproliferative category as well. So, and then the WHO has been updated and is being updated again and the big piece is that they've now recognized cytogenetics as an integral component to understand disease. So, everybody gets cytogenetics done as a part of their standard workup and even as you continue to have bone marrow biopsies, they will look at your cells to see. Can the cytogenetics go to normal if you had an abnormality? The answer is yes. Can your cytogenetics go from normal to abnormal? The answer is yes. So, it's always checked and that's a long wait for a results. About three weeks to get that result whereas the hematopathology report, you'd probably get in a week. So, they look at AML. They put that in there as well and lots of other categories. So now, we've gone from five categories in the FAB to over 17 categories in the WHO classification system looking at things that are unclassifiable and poorly described. RCMD stands for refractory cytopenia multi lineage dysplasia. That means you've got a couple cell lines down and dysplasia, again, abnormalities. So they look different and then the U just stands for unclassifiable and then you begin to see that deletion 5Q in there. So, there is a certain MDS that only has 5Q-. So, here's another quickie. When you have chromosomes, all of us have chromosomes, and if I say that I have normal chromosomes it

means that I have 46 chromosomes. I have 23 pairs and I get my genetic material half from my mother and half from my father and they're labeled one to 23 and they have two components to being a chromosome and they only have arms. Chromosomes don't have any legs. They only have arms and so they have P arms and they have Q arms. So, the P arms are the petite arms and they're the ones on the top and the Q ones are the ones on the bottom. So, if somebody says they have a 5Q- it means that on the Q arm of the fifth chromosome... if it says 5Q- then it means the entire Q part is gone. Why would that be significant? Okay. So, I drive a car and I go to get my car in the parking lot and when I get home tonight and the front quarter panel in my car is gone. Is my car the same car as when I left it? No. Is it going to function like it should if it was a whole car with a whole front quarter panel? No. So, if you remove a piece of a chromosome that's helping to create your blood cells, do you think they're going to function the same way? No. Absolutely not. So, huge, huge significance when even you have small abnormalities. Then we talk about dysplasia. That's like how different does it look and then the number of blasts in it. So, all of it talks about classification systems. So, lots of information in there, but that's where it comes from.

Now, someone at lunchtime was talking... Oh, question.

Q56: Is what you're putting up there, is that available in our material or on the Foundation website or anything like that so we don't...

Jean Ridgeway: I think so. Dee, is this stuff in there?

Dee: (inaudible 2:12:53)

Jean Ridgeway: She says page 13, How is MDS Classified? I'll give you my E-mail because I can actually give you the article... I wrote an article. Anyway, in the article I put this together, so if you want my E-mail I'll give it to you and then I can just shoot you a PDF of the article if you'd like, but yeah that information is in there. That's okay. Alright.

Q57: It seems like a lot of the... It's always the Q arm that's missing. Is there a reason for that? Do you ever see the P arm being (inaudible 2:13:37).

Jean Ridgeway: Oh, you'll see... That just 17P deletion, Trisomy 8 means you have three 8. So, you should only have two pairs in number eight and then if you have three, then they call it Trisomy 8. Minus 7, some people just whoop seventh chromosome all gone. Oh, there's so many and when we look at this IPSS classification, you'll see that some are very specific and can mean good things or could mean not so good things or it means... we don't know what it means. So, there's lots of things out there about it, but not one abnormality is consistent in MDS unlike with some other diseases. There's a disease called CML that definitely has only one problem, a piece from 9 and a piece from 22 switch places and that's the classic abnormality in that disease, but not so in MDS.

Alright. Prognostic scoring system. So, what does it mean? So now, you have all... Okay. So you get the diagnosis and you find out all these things about it. So, what does it mean and how does it relate to your diagnosis and how long are you going to live and what should you be treated? Shouldn't you be treated? So, that's where this scoring system comes in. So, there's the International Prognostic Scoring System and then there's the revised scoring system because it's been around since 1997. So in '97, there was really no scoring system and people who were very interested in MDS got together and they looked backwards, so they call that retrospective and they said what can we figure out from all these patients that is going to help us understand how does the disease behave and so they looked at everything. They looked at ethnicity, they looked at gender and the three things that they came up with that could help them understand the disease were how many cytopenias do they have? What are their cytogenetics and how many blasts do they have? And that's what created the IPSS scoring system. Now, just a couple of years ago that system was "updated" to include more cytogenetic information and to look at does transfusions play a part in understanding how the disease is going to behave. So, these are actually... the IPSS and the IPSS-R are you can actually get the journal article. So, the hematology journal article if you wanted to get it. If you go to the MDS Foundation website, you can get a link to this article. You could take a picture with your iPad, too, but those link right into that. Now, some of us because of the work we do in clinic have the app on our phone and so when a patient comes in and sees us in consultation for a second opinion this is the information that we look at. We'll pull their old bone marrow... whatever they bring with as far as records, we'll go ahead and plug these in. Now, someone at lunchtime asked me can it ever change and that's one of the criticisms of this prognostic scoring system because in general it's done when you're diagnosed. Now, your disease may be stable or it may change, but this is really done at the beginning of therapy. It's in general not done again because that's not where it was tested and where they have shown that it's been valid, but the IPSS scoring system has a lot of people not happy because of some components and where they... just some of the data that they didn't include or did include.

Alright. Quick fun facts about MDS. If we were playing MDS Jeopardy, we'd say what's the average age and you'd say, "Alex, I know. It's 73," and it remains an incurable malignancy for the majority and what's the cure for MDS and we talked a little about it and it's an allogeneic stem cell transplant. That means your donor is someone not you. So, it's not an autologous donor. You're going to use another donor source and there are lots of donor sources. The first thing you would look for is a sibling because I get my genetic information from my mom and dad and so do my brothers and sisters. So, you have about a 25 percent chance statistically of matching a sibling. If you have one sibling, it's the same if you have 10. You increase it a little bit, but not so much and if you don't have a donor then people... the data gets analyzed through something called a registry. So people who have volunteered to be part of this registry, they've done the cheek swab to see who's the baby's daddy, but this time it's like will I be a bone marrow donor and all they do is swab the inside of their cheek for constitutional DNA. So, those folks are also part of the registry and that is an anonymous process. Once that's done, the folks who actually work in that component of the program where if you're going on for a stem cell transplant they can know what country, what gender the patient is in general and at a year mark, you can write a letter to your donor and the donor then can write a letter back to you. So, they're very much

protected which I think is a good thing, but that's how the process goes and then there's also umbilical cords people use for transplants as well, but what happens about... If you're looking at causes of death from MDS, the disease itself really is responsible for the majority of why people die and the other thing you need to really consider that I think sometimes we put binoculars on about is that we blame everything on the MDS. We don't want to blame anything on kind of normal aging, be it arthritis, heart disease is a problem for our country. People have diabetes. There's lots of other things that enter into the picture when people get diagnosed with MDS and being part of underneath good medical care helps improve all those things.

And what about how do we pick those treatments and so Dr. Walker talked about risk stratified and that basically means understanding where a person is with their disease is going to help you tailor for individual therapy. So, somebody who has low risk disease who doesn't get any transfusions is approached and discussed with different treatment options than somebody who has a high level of blasts and getting transfusions, say, three times a week. So, they're very, very different and in general when do we begin to treat people? We begin to treat them when the disease starts to need treatment, need attention. Are people becoming transfusion dependent be it platelets or red cells? Every situation is a little bit different. Are people having "symptomatic" cytopenias, shortness of breath, headaches, bleeding? Infection is another big problem for folks who have MDS and some people actually get diagnosed with MDS because of infections. They may have a pneumonia in the fall and then they get a skin infection. They could have an ear infection. In primary care, they don't draw CBCs. That's not what they do. We do that in hematology. They check your cholesterol. We don't really care about your cholesterol. But it's not done in the community setting. So oftentimes, the road to get diagnosed to MDS can be very difficult because the problem is not really being identified early enough for you and I don't know how true that is for the folks in this room, but that is a very common theme that you hear from people that it takes a while to get the diagnosis because of how difficult it is to sort it out.

Other things about treatment. Performance status means how active are you? So, there's actually a couple scales of performance status. If you're up and about and you get dressed that means you have a good performance status. If you spend more than half of your time in bed, that's not so good. If you spend all of your time in bed, you're unable to drive, you can't pay your own bills then that's called a poor performance status and there's a scale that goes from 100 percent to zero. So, 100 percent is you're all independent. Zero is you're pushing up the daisies, but 50 percent is you're spending at least 50 percent of your time in bed. So, that's kind of the cutoff when they look at that and then comorbidities were those things that I mentioned. Other medical issues. Do you have diabetes? Are you have COPD? And then looking at risk categories and do you have primary versus secondary? You had mentioned that a little bit about prior treatments either be it radiation or chemotherapy. That would be a secondary or a therapy related MDS and then what about your cytogenetics (inaudible 2:23:05) and what about your lifestyle.

So, what are current treatments? We talked a bit about this. Transfusions. Correct? We talked quite a bit about that. I don't know if there's any other questions about transfusions and then growth factors. There's a couple different growth factors out there. There's the growth factors for

red blood cells called Erythropoietin or EPO. That's the short form of it. That's that red cell hormone and then there's something called Neupogen and that's a white blood cell hormone that will boost up your white blood cells. Sometimes they're used together. I heard Dr. Walker say to somebody maybe they need to combine the two because they act synergistically. So, it's like they potentiate each other and then there's a number of... So, there's three approved therapies for MDS. One of them is a pill. It's called Revlimid or Lenalidomide and that drug is a cousin to Thalidomide. You remember Thalidomide? You hear about the babies who were born without arms and so what they found out was that why were they born without arms is that it stopped the blood formation and it stopped the growth of these little fetuses and so they took that knowledge and morphed it into using it in cancer cells to decrease the signaling for the cancer cells. So, that's why it's been successful and they call it an immunomodulation drug or an IMiD. So, Thalidomide was the first drug out and then Lenalidomide has been the 200 times more potent sister drug of that and then there's a new drug, a newer and improved even more so than that. It's called Pomalidomide and that's not yet used in MDS, but it's used in multiple myeloma. Then we look at 5-Aza or Azacitidine and then a drug that's very similar to that called Dacogen or Decitabine. So, Azacitidine is approved either for injection or infusion. So, you can infuse it via a line, an IV line or if you have a portacath you can do it that way. Decitabine is just given as an infusion and then there is different chemotherapies to be used. Cytarabine is something that's used very widely in Europe. So, it can be given as an injection. It molecularly is very similar to Azacitidine. So, they're just a couple molecules away from one another and it can be given as a subcutaneous injection and they use it quite a bit in Europe. It is not as effective as Azacitidine, but Europe practices almost exclusive national health care. So, what do you think drives national health care? M-O-N-E-Y. So, what are they going to choose? They've chosen as gatekeepers to give that as a recognized therapy, but I will tell you that people with M-O-N-E-Y still buy it. So if you're fortunate enough to have a secondary insurance and you live in Europe or Japan, you can buy that medication and then we looked at bone marrow transplant and then we talked quite a bit about investigational agents. In this really busy grid... Go ahead.

Q58: For the Vidaza, what determines how many rounds, is two rounds or when you need to stop that course of treatment?

Jean Ridgeway: So, his question is how many rounds, who determines or what determines it? So in medicine what people like to do is practice something called evidence based medicine. So, show me the data. When the original studies were done... when Azacitidine came out there was a study and it was a phase three study and it looked at best supportive care versus Azacitidine and patients had bone marrows like almost every month or every other month, but what they found through that study was that people had to have at least four if not six cycles to get a response. So that translates into most providers will say we'll give you four to six cycles of Azacitidine and then do a bone marrow to see if you've had a good response. Now if you've had a response what we do know in that study what happened was people who had a response... Now, that study was also given for seven days. I heard some people talking about do you get it for five days? Do you get it for seven days? The purists in medicine will say it was given for seven consecutive days. I give it for seven consecutive days. So however that happens in their

clinic setting, I'll tell you in my clinic setting it doesn't happen because we're closed on the weekends. We don't have a clinic to do that and some of my docs will do five days only, some will push the two to subsequent Monday and Tuesday. Some will just do five and there's been some other studies with that. So, look at... Going back to your question, how many/how long. So with that study, four to six was shown for a response even an initial response and but after people got a response, they were allowed to continue and then they had to stop. That was the design of the study because they didn't know would it be harmful to give them more? So when in that situation people stopped getting the drug, but what happened was that people relapsed and at that point in time the drug was only available through clinical trials and the NCI actually had a supply of the drug so we could petition with the NCI and get the drug for people. It was quite a lengthy process. So, we give it for four to six cycles and we know that now people should stay on the drug as they continue to benefit. Do people lose their response? People do lose their response. When do they lose their response? Hard to say. (Attendee)'s husband has been on 30 cycles of it. I have a patient who's been on 38, but there are other people that it's not so true. What happens if you stop? Sometimes people say, "You know what? I'm better. No more transfusions. I want to go to Venice. See you in September," and I think that's a personal decision. Can you rechallenge somebody when they come back? The answer is yes. Can you guarantee they're going to have another response to the same drug? You can't guarantee it. In our experience is people will have a vacation. Sometimes we'll even switch if they've been on it a long time and we'll go to five weeks or we'll go to six weeks and sometimes people's biology of their disease says I don't like the six weeks. Their blood count starts slipping whereas before they were transfusion independent and then they start dipping their selves and then will go backwards and we'll go back to the four weeks. So, it's a lot of manipulation and expertise of the provider in what they'll allow you to do. Does that answer your question?

Q58: You were saying that they check bone marrow after four to six cycles with Vidaza?

Jean Ridgeway: If you're not on a clinical trial, your doctor may not do that.

Q58: Would the improvement show up in your CBC prior to that?

Jean Ridgeway: It probably would. It probably would. So, it really depends. If you're on a clinical trial or if you work with people who are... They really want to know because sometimes there's not a one to one correlation with what your blood counts are showing us versus what's in your bone marrow or you want to be able to document that wow, this person has normal cellular, a low number of blasts and no dysplasia. Maybe you really want to be able to concretely document that. There's something called the NCCN guidelines. Have you ever heard of those? So, there's something you might to write down. It's called NCCN.org. The NCCN.org is the National Cancer Comprehensive Network and what they represent for every disease, lung cancer, prostate, GI whatever is the countries' experts in that disease and they will write a review, the whole panel of them like 20 and they review it usually twice a year and they make recommendations and we find that industry follows the NCCN Guidelines for recommendations for best practice. So, I heard somebody asking about what's the best practice. A lot of people

look to the NCCN guidelines and so you can look up in there and you can get the MDS one about it and what it has to say and so there's something called algorithms. These little charts if a then b then c kind of thing, but then there's also a narrative and so in the NCCN Guidelines I'm trying to think of it says... it may be like highly recommended that you do the bone marrow at that point in time, but it's not definitely needed. Other questions? Wait. Let me look at my watch.

So the white blood cell hormone is called Neupogen or G-CSF, granulocyte colony stimulating factor. Neupogen. N-E-U-P-O-G-E-N. It's trademarked by Amgen and there's a long acting one, too called... Oh, I'm not going to be able to... I totally forgot. Neulasta. N-E-U-L-A-S-T-A. So, those are sometimes used. Let's see. Busy, busy but we won't... I think she spent a lot of time talking about what's new and how do things work and these are drugs under investigation. So, if you ever get sleepless and you want to go on the Internet in the middle of the night, you can go to NCI which stands for the National Cancer Institute.org (nationalcancerinstitute.org). You write the word 'clinical trial' and then you pick a disease and you start looking and it will come up and it will give you descriptions of all the clinical trials available from Washington to San Diego. So, it's a very comprehensive. They'll keep a list of what are they, who's doing them and remember she talked about that eligibility criteria or what do you need to go on this study. It'll list that as well. So, lots and lots of therapies under investigation and the more we know about MDS and the more medicine goes forward what we're finding is that the drugs are becoming very specific and very targeted and a lot of them are also becoming oral and when it's in clinical trials that's great. When it rolls into a commercial setting when it becomes approved like Lenalidomide drugs are unbelievably expensive. Has anybody in here been on Lenalidomide?

Q59: I'm on 5 mg for 11 pills a month is \$4,500. Now, once I meet my \$6,000 deductible it's zero, but when I was on 10 mgs in 2011, it was \$8,900 a month.

Jean Ridgeway: So, mgs means milligrams. So, the pills come in different forms, but very expensive. Very, very... and sometimes companies are able to get some patient assistance for you, ie. really cut down... but who can afford \$5,000 a month? That's just for 1 pill. It's unbelievable.

Q60: I have a question about that. Our hematologist is hinting that he's going to recommend getting into a clinical study for that drug.

Jean Ridgeway: With Lenalidomide or Revlimid?

Q60: But it's a new variation of it.

Jean Ridgeway: There's a couple of them out there.

Q60: Here's my question if that would be what we choose and (Attendee)'s in that clinical study what happens when that's over? How does she get the drug then?

Jean Ridgeway: So, when these drugs are in development and they're looking for clinical trial participants they will supply you with the drug and usually in the protocol it will say will continue... they'll write it a couple ways. They'll continue to supply it even after it gets FDA approved for X amount of time for no charge for you because you were kind enough to participate in the clinical trial. So, that's... and sometimes they'll say we'll supply it for 10 years. So remember I told you about CML. So, that drug is called Gleevec or Imatinib. That was one of the first targeted therapies approved in hematology and people who went on that study were guaranteed free drug for the rest of their life. So, and there are people that are now... Let's see. That was approved in 2002, I think, and they're still on the drug. So, they're not paying for it. There can be some real positive things about going on a clinical trial.

Q60: Yeah. Yeah. Because I was concerned if she did it and it was over and had to be \$10,000 a dose which is about what it is. It's like huh?

Jean Ridgeway: Right and you ask those questions and they'll give you a document called a protocol and a consent. They'll give you a consent and in the consent which is usually a really lengthy document about 20 pages, but it's written for patients and so hopefully it's written at a sixth grade reading level, ie. so you can understand it and it'll have bold how long am I going to be in this, what's expected of me, etc. and those things should be spelled out and if not you ask them. So, there are... the good thing is that there are lots of therapies. Vidaza was approved in 2004, 10 years ago, and I told this to someone else early in the '70s and '80s and I have been doing this since the '70s and the '80s people who looked at Myelodysplastic Syndrome and studied in it were looked at by other hematologists as quacks because they were like, "Oh, it just happens when people get older. There's really no science behind it," and so the naysayers have been proven in error, but so the drugs for Myelodysplastic Syndrome in the whole era of knowing about this disorder has only been 10 years... 10 to 15 years. So, 10 years this year for Vidaza to be approved. So in 2006, Decitabine or Dacogen was approved. So, these drugs are relatively new on the market and I think a lot of the questions that are out there, Dr. Walker showed a slide about does giving Azacitidine before transplant impact survival or something. That's a new question because the drugs just haven't been around even though 10 years sounds like a long time, it's not such a long time.

So, we talked about transplant and what about age? Different centers have different age parameters for transplant. I mean, honestly, if you don't need a transplant you don't get a transplant. It's not a benign therapy. It's a very intensive therapy. Basically, 30 percent of patients who get transplanted don't make it to 100 days. That's like all comers over 50. So, there's what we call a 30 percent mortality. That's pretty high. That's staggering. It should make you evaluate and take your breath away, but we will... I'll tell you that we transplant at our center because a few of us really have an interest in older patients. We have a big cohort of patients who over 70 who have been successfully transplanted. One of our gentlemen with acute leukemia was 76 and he just underwent... he was a very fit guy and so he had acute leukemia and underwent a transplant.

Q60: Is most of that mortality due to rejection?

Jean Ridgeway: No. No. Infection. So what happens people can get just these overwhelming infections after transplant because you need to totally... you need to get rid of everything. A lot of transplant centers do something called... some people say minitransplant. That's kind of a funny term. That's like almost pregnant. It kind of doesn't really hold any water. You are or you aren't. Right? So, it reduced intensity means what the combination of drugs that they give you before they infuse the stem cells. So, that's what it comes down to and with older patients, I mean, if you're 76 and heading into a transplant the chances are of you having some other concomitant health conditions is pretty great. I think in general you can probably think about a lot of your friends who are your age who are in better shape or worse shape and think of them going forward to a transplant. You'd go, "Ooo. I don't know about that." So, the better shape you're in when you go forward for a transplant data tells us, we live on data, we live on evidence. The better the shape you're in the better you're going to do. It is a successful therapy, but it's something to be taken with great seriousness. So when the transplanter said, "I hope I never see you." That's exactly what you want to say. I hope I never see you either. That's not what you want to do.

Anyway, what else do know about when people enter therapy? So if you think about that bone marrow... that picture a long time ago about if you've got all these malignant cells now in the bone marrow and your other cells are depressed, if you start removing all the malignant cells, you basically have removed the driver to create hematopoiesis. So, what does that mean? It means if your malignant cells are causing blood development even though it might be a little bit, if you start suppressing the malignant cells your counts are going to get worse before they get better. That's what that means. So, you'll see your counts here and then you'll see dropping and then you'll see better. People who get started on treatment, I'd say that probably 50 percent of them within the first four to six weeks may get an infection or may be hospitalized during that first month of treatment because you're going to get worse before you get better but then as you go forward things get better and sometimes it's hard to be optimistic and hopeful as you're really feeling worse when you should be feeling better because probably at the time you're starting therapy you may not feel really great. If you're getting a lot of transfusions and things have kind of come upon you in that way, but being proactive in the management of those side effects can just help you do better for longer.

So kind of finishing up because we're almost finished. My watch says it's 10 till, but that's not right. It's quarter till. Right? So what happens in the bone marrow? So before the treatment begins when you look at this little slide, those spidery looking cells, those are bad cells. The big red discs those are your hemoglobin cells and then those other purple cells, those are some normal white cells but then there's some dysplastic cells in there, but so as you start before treatment then the blood counts drop as the MDS can progress and because of the abnormal stem cells and then you're given treatment and things kind of clear out. So, the second component there looks a lot clearer. So, there's not so many of the white cells and then the little crabby kind

of look is the same and then you also look at what's going on with the neutrophils. So, Dr. Siciris (sp? 2:43:24) and this is actually a graph of a combination of a number of patients. So, the absolute neutrophils and ANC that's... the neutrophils are the most important white blood cell. Eighty percent of your white cells should be neutrophils and that protects us against bacterial infections. So when you get treatment what happens, boom, it drops and see at that six week mark? That's when it's really low and then it begins to go up after that. So, start it at about week 11 and then look at week 16 which would be four months. Things are really beginning to level out and so this is all driven by lots of other patients who have gone through therapy and then you start seeing the blood components in your bone marrow begin to normalize and then they repopulate with better cells and hopefully as things continue to get better then the number of transfusions stop or at least decrease and people begin to feel better. So, that's in the book, too.

So, early toxicities. When we talk about side effects some people call them toxicities and I'd say that these are... this the hard part for people. Again, you're not feeling great. You still got to come back to the clinic. Maybe you got a fever. You might get hospitalized. That's when it gets kind of hard and that's when you need to say, "I just need to keep going," and push forward with it. So this is kind of busy, but basically to answer your question what's the minimum amount of time? Four to six cycles.

Other strategies of getting through what happens. Yes, there are and they're relatively standard. Sometimes people have to be delayed a bit because maybe they have pneumonia or something or the dose has to be adjusted because the blood counts go too low because remember in order to really give you the most therapy we have to be able to adjust those things. So, you may get dose reduced and then brought back up to a level if you've gone too far down with your numbers and then setting expectations. Knowing that things may get a little worse before they get better. If you know that that's normal then I'm hopeful you won't be as nervous.

So, this is a patient and let me explain this to you. So, this goes from June of 2010 to July of 2011 and the purple boxes are hemoglobin and the platelets are the yellow triangle and then the really dark purple is the white blood count and so this person started with therapy and so some people say that when you start the therapy you kind of want to fix the factory. So, you can't get a really good product off the assembly line unless you fix the factory. So, giving people therapy people say let's fix the factory to get a good end product. So, you can see this person's hemoglobin. Even when they started was pretty robust. Twelve grams per deciliter. That's pretty good. The white count not... It's like $4 \frac{1}{2}$ and the platelets are very, very low. So, they're like down under 20,000. You can tell that by on the right hand side that's where the platelets. So, you can see this person kind of before and then there's cycle one. Things stay kind of slow and low. Hemoglobin drops up and down, but the take-home point is when you look at the far right hand side of the graph and 100 after cycle four, this person's counts had dramatically improved, but it took a while to get there. Now, this is a patient who did go onto transplant and then even post-transplant their counts are even better, but this is a patient that gets followed out in Arizona, but that's actually somebody's blood counts.

Here's a person who was on Lenalidomide or Revlimid for 10 years. So when these... Again, this is the therapy what was introduced in the early 2000s as a clinical trial and Dr. Allen List did a lot of work with that and Sandy Curtain is his nurse practitioner and this person started out in what we know about people who get Lenalidomide is it can help the red blood cells more than anything and you can see that all the way to the left 2002 to all the way to the right to 2011. So you look at his hemoglobin how it dropped to 8 ½ or so but then after a few months this person has maintained their hemoglobin as a relatively normal 11 grams per deciliter and the platelets again, those yellow triangles. He's continued over time, but slowly to gain a normal platelet count and the white blood cells are... they've dipped down at the beginning but he's maintained a low level of normal blood counts. So, can people be on these therapies for a long time? Yup. Can they get normal blood counts? The answer is yes. So, 10 years this person... She has more... This person happens to keep a copy of their own... I know this person. He's an engineer and so he keeps a copy of his own.

And then the last piece we talked about. So, how do I stay healthy? What can I do? Balanced diet, being active, live life. You're here and so be healthy, be active, be as active as you can. You want to avoid infection. We talked about everybody getting a flu shot. Avoid bleeding. Well, that's pretty interesting, isn't it? But really enjoy the things that you love. Live your life. Go do what you want to do. Feel well and go out. Get enough rest. Rest is important, but activity is important, too. Thirty minutes a day is the new recommendation for being active. So, that means walking, like vigorous walking. So when you walk, you want to move your arms and get walking. Swimming is a great exercise. I don't know how many people are like really neutropenic, but if you're allowed to go swimming, I would say swimming is a great exercise as well and lots of resources. So, *The Building Blocks of Hope* is definitely one. I saw someone... the book, *The Hundred Questions and Answers About MDS* is another great resource. The Leukemia and Lymphoma Society has a little book about MDS. That's another great resource and be an active participant in *The Building Blocks of Hope*. Healthy Body Healthy Mind... These are a couple websites and these also are... you can get these from the Myelodysplastic Foundation. There are a couple little videos. They look like YouTube videos. I might come back to them. Hang on a second. So, *Becoming a Partner* it, this *Building Blocks of Hope* is really... it's global. I don't know how many languages it's been translated into, but I think over a dozen languages and symposiums like this are held all across the world because it's not a disorder that's confined to the western culture. In Japan and in Asia no matter where you go people are living with this disorder and because of movements within groups like this, people are getting better care and very standardized care. So, that's a good thing. Remember that this is online and you can have the whole... If you don't have the handbook, you can go online and get it and it's got different features if you go online that will link you into video thumbnails. So, it has that little graph of... Are you leaving? Why are you leaving?

(inaudible 2:51:32)

Jean Ridgeway: Why are you leaving (Laughing)

(inaudible 2:51:40)

Jean Ridgeway: She got to take (inaudible 2:51:42)

(inaudible 2:51:43)

Jean Ridgeway: My flight. My flight.

(inaudible 2:51:46)

Jean Ridgeway: Right.

(inaudible 2:51:51)

Jean Ridgeway: Thanks, Dee. Bye, Dee. I'll see you soon. I have to give her a hug.

So, the other thing in the handbook you can create if you want to keep track of your blood counts and they also have an interactive piece if you like to keep them in an Excel spreadsheet. They have some of that as well. So, this is just... If you want to create a personalized plan, it's on page 92 to 98. Now, I really feel like a teacher and then Tracking Your Progress and you can put it on your iPad, you can put it on your Kindle. So, they just want to make sure that they've covered all the electronic resources to get the information and here's the number. I would imagine most of you have somehow known about the MDS Foundation otherwise you wouldn't be here. Or you just put in MDS Foundation and this is just the format of the book. There's a couple different sections. One's Understanding, Looking for Treatment, Quick Tips. Talking About Iron Overload and then your plan for that. So, I'm zipping through this because like I only have three minutes and then you're looking at the MDS Foundation. It talks all about that and then that's you. I want to go back and see if I can link in... I think I'm on the Internet. So, let's see if we can link... So, this is if you went to this one website and it's an interactive little loop about new ways to manage MDS and they interview people and it talks all about it. So, it's Healthy Body Healthy Mind. Let's see. I'll go back... if you want to write the website down. Oh, dear. Hang on. Here it is. Oh, gosh. So, it's itvisus.com. I think if you put that in you should get it. Oh, you have the little card in there? Oh, it's a CD, so it's in your packet. Okay.

?: (inaudible 2:54:17)

Jean Ridgeway: Very good. And that's just...

?: (inaudible 2:54:25)

Jean Ridgeway: Okay. There. See... Okay. There you go. Well, questions? What kind of questions do you have? Questions? Comments?

Q61: Hello.

Jean Ridgeway: Where are you? There you are.

Q61: Is there anything being done to create more awareness of MDS? I'm sure there are folks out there that are wondering around with it.

Jean Ridgeway: Oh, sure. So, I think one of the... You've heard of Robin Robins? Right? So, she had MDS and she had a sibling transplant. Correct? So, I think...

Q61: She has a new book out.

Jean Ridgeway: She has a new book out. Right. So, I mean, there's nothing better for a disease than a celebrity to get sick because they can be very vocal and I think the exposure because of her notoriety has helped raise some awareness and now because of hematology... He's got a picture of it. Very nice. I haven't read it though.

(inaudible 2:55:29)

Jean Ridgeway: Okay.

(inaudible 2:55:37)

Jean Ridgeway: Did you see it?

?: Yes, I did.

Jean Ridgeway: What did you think?

(inaudible 2:55:44)

Jean Ridgeway: That's something, but communities...

Q61: I live in a community or a county of maybe 60,000 people. This only happens to one out of... or two or three out of every 100,000. So, maybe I'm the only one in the area.

Jean Ridgeway: Yeah. I mean, it is a rare disorder. It's still considered a rare disease, a rare malignancy, but physicians are being trained from a hematology perspective to recognize this and they're trained accordingly to give good treatment to patients. That's a huge stride because 25 years ago that was not true.

Q61: The other issue every time I see Dr. Tu, he talks about funding for MDS research. I wish there was some way...

Jean Ridgeway: The funding across the board from the federal government I think just looking at budgetary issues, the National Cancer Institute, I don't know how many millions of... tens of millions of dollars got cut period. Really probably the most effective way to help visibility of the disorder is to write a letter to your local legislature. I don't know if it's a senator or congressman and you can tell them... I mean, they really do respond to constituents' perspectives and we talked a little bit about ESAs before, the Erythrocyte stimulating agents, the EPO and the Darbos, a few years ago... I'll go backwards a little bit for you. They were very popular and they were used probably inappropriately by a lot of medical practitioners and there was a group of patients who had strokes and they died from it. Now, they were not MDS patients. They were patients receiving chemotherapy because if you think about it when you have a lot of red blood cells your blood could be thicker. So, people could be prone to a blood clot and so there were some patients with head and neck cancer who were receiving chemotherapy who received Erythropoietin and they had heart attacks or strokes or whatever and so things were put on hold and now it's very restrictive even for a prescriber to write... for the patient to get it. You have to meet certain criteria and the CMS which is the people who control Medicare allowed MDS as a disease to be relatively untouched by all the really severe restrictions of use for the Erythropoietin because patients went to Washington, DC and stood up and advocated for themselves and a big group from the MDS Foundation with some of their patients went there and argued before Congress to keep it protected. So, they will listen. Somehow you can go online and find out who your legislature is but send them a little note. It is a rare disorder. It is.

Q62: (inaudible 2:58:57) from Vidaza and it's a 10 year anniversary. Who do we thank? I mean, the drug company? The researchers?

Jean Ridgeway: She talked... The very first slide that Dr. Walker put up about Vorinostat and 5-Azacitidine done by Louis Silverman. Louis Silverman was the principle investigator on the first study that was done with Azacitidine back in the '70s. So, he's at New York. Louis Silverman is his name and it was very interesting. I mean, I work in an academic institution like Ohio State. So, we have a lot of clinical trials and so part of... I didn't want to say bias, but part of how patients come to us is because they need a clinical trial. They've seen their regular physician and they've gotten treatment locally, but now they need something different or something else and so we have a lot of clinical trials and so there are actually groups of clinical trial people. They're called consortiums and we were part of that study and... So back in the late '70s and early '80s, we were part of that study and patients actually got the drug comes in a little vial and it's powder and then you have to mix it up and so we used to teach patient show to like mix their own chemo and they gave it to themselves at home and when the study completed, the pharmaceutical companies originally said oh like nobody gets MDS and nobody wanted to pick it up because they didn't see the profit in it because they said it's such a rare disorder how can this ever... will this really happen and so there was one company that originally... I don't know if you buy it from the NCI, but somehow they were granted rights, etc., and they've since been bought out by another big company and now the drug is generic. So, it's lost its patent, but it was the second big company to pick it up was Celgene who also holds the patent on Lenalidomide. I mean, it's a

big pharma company, but big pharma has money. You can't do these things on a wish and a prayer. They're very expensive and the usual time from bench to approval is about 17 to 20 years. So, that's a lot of time and that's a lot of resources. So, yeah. It's in the billions now that it really costs a drug to come to market. So, it's a rare disorder and if I'm a financial entrepreneur, I'd probably want to put my money where there's going to be a lot of it and not a little of it. It's very interesting. I mean, that's another side of medicine. A whole another side of healthcare. Any other questions? So, somebody around here wanted to get names of people who were kind of in the area. I don't know if you were able to connect to do that. A couple people. Okay. Let me give you my E-mail. If you want to get a hold of me, send me an E-mail because I never answer the telephone because I'm never at my desk. I'm always in clinic. So, let me give you... So, it's... my name is J is my first initial and then R-I-D-G-E-W-A they cut off the Y and it's @medicine.bsd.uchicago.edu or you can probably pick me up off the MDS Foundation webpage because I'm also on there. Well, I hope you're going home with... a little bit better insight, a little bit better understanding. I think I might be on the MDS website. You could Google me which is kind of creepy, but that's okay. I am listed on there.

(inaudible 3:02:47)

Jean Ridgeway: Oh, I will.

(inaudible 3:3:02:50)

Jean Ridgeway: I'll share with you that my doctoral project is looking at patient education for patients undergoing an allogeneic stem cell transplant, so to help people understand the myriad of care needs that they have as they go through that situation. So, that's what I'm doing my thing in. So anyway, have a great day and thank you all for coming.

(Applause)