Speakers:
Timothy Graubert, MD
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Susan Hogan: My name is Susan Hogan. I'm Operating Director of the MDS Foundation and you might have met… we also have Tracy Iraca, our grants director, outside. Thank you for joining us today. Just a couple quick housekeeping notes. A couple of you mentioned about the parking validation. There'll be a gentleman from the conference center coming up at lunchtime. So if you have your tickets, we'll make sure he stamps them so you get the special parking validation price and also you probably already know but the restrooms are located downstairs. So, there's an elevator right next to the table out there. So if you, you know, or else the stairs whatever's more convenient and just quick I'm talking into the microphone now. When you do speak, could you remember to press down… speak into the microphone because we like to audiotape the session and we want to make sure we capture everybody's comments.

In case you're not too familiar with the Foundation, we're located in Yardville, New Jersey. It's a small town, but our reach is worldwide. We have Centers of Excellence all over the world and for the past 22 years we've been devoted and dedicated to the study of the Myelodysplastic Syndromes, offering support to patients and educational programs to healthcare professionals and caretakers worldwide. We have a great agenda in store today and we'd like to thank Dr. Tim Graubert and Jean Ridgeway are presenting from Massachusetts General Hospital and Jean Ridgway who's a member of our Nurse Leadership Board at the Foundation is going to do the nursing presentation. Also immediately following our event, there's going to be if you want to stay at two o'clock right in this room there's another little… it's an opportunity for iron overload and transfusion information. It'll take about 45 minutes. So if you just like to stay on your perfectly welcome to do that. We have our breakfast in the back which you found and we'll have lunch at around 12:00. We'll be flexible. It depends on your questions and answers. Please feel free to talk and share your interest and your information. So again, a very warm welcome and I'd like to thank our supporters Baxalta, Novartis and Celgene for making days like this possible and I'll now turn the program over to Dr. Graubert.

Timothy Graubert, MD: Good morning, everybody, and thanks very much for that intro. Thank you all for coming sacrificing some a few hours here on a beautiful Saturday afternoon. I really enjoy doing these presentations. I've been taking care of patients with MDS and doing laboratory research for about 30 years and my laboratory really focuses on this disease. So, I really welcome the opportunity to talk to the real folks who are in the trenches and hopefully provide some new information, review some of the basics and address questions you may have.

We received a few questions in advance and I added a few slides and tailor it a little bit to try to address those, but I will stick around throughout the program through lunch and so forth. So, if there are things that I confused you about or stuff that I just didn't address or you have ongoing questions grab me later. I'm happy to talk to you some more and this is a small enough group

that I hope we can make it interactive. Don't be shy. Raise your hand if I mumble, bore you, confuse you or if you just have questions. Please, the whole point is for this to be valuable to you. I have too much information, too many slides to get through. So, I don't expect to get through everything. So, I don't at all mind if you stop me and we go off on tangents. Again, that's why I'm here, but I have to kind of hang out over here because I can't advance the slides from here.

So, this is how I organize things generally in terms of slides. I'm together the first half or so really focusing on issue of making the right diagnosis, how do we do that once we make a diagnosis of MDS, how do we then sub classify because as you know MDS, the 'S' stands for Syndromes which means this is not one disease. This is a collection of a number of diseases that have similar features and it's pretty important to really for an individual patient to be subclassified into the right subtype of MDS for reasons that you'll see. So, we'll go through classification then risk stratification or prognosis. Again, I'll emphases how important that is. So, that's kind of the first half and then the second half is about therapy. Very quickly what are our standards, what's our overall approach as we look at patients with MDS and think about therapy, how do we generally conceptualize the right path they should go down, what are the standard therapies available and then where are going, what's on the horizon and so it's a lot to cover and different parts of this is going to be important to different people.

So, we're starting with the diagnosis. So, here's in 2016 how we make the diagnosis. You don't have MDS if your blood counts are normal. You have to have abnormal, essentially low blood counts and it can be just one of the three different lines that we look at, the red blood cells. So, just anemia; or just low platelets, thrombocytopenia; or low white cells, neutropenia or any combination of those, but you must have an abnormality in your blood counts first. That's essential, but that's not enough because many other things can cause any one of those findings. So, you need something else and this is where, frankly, it's pretty murky. The so-called decisive criteria are not so decisive in my mind largely rely on us looking at cells from the bone marrow under a microscope and deciding whether or not they look funny in a nutshell. There's a little bit more to that, but the point is there's a fair amount of subjectivity and therefore honestly disagreement between different centers about these criteria, but that's where things stand today. I think that this is changing, but it hasn't changed yet.

As you know, MDS has a tendency to evolve sometimes rapidly, sometimes slowly into acute leukemia, AML, acute myeloid leukemia. It happens overall in a little less than a third of patients with MDS. So, it's not a certainty, but about 30 percent or so will at some point evolve and that, again, we're talking about diagnosis. That's pretty clear cut because that comes down to counting blasts, the immature cells in the bone marrow and that's pretty iron clad. There's not that much subjectivity and disagreement there. If you gave 100 cells to five different pathologists to look at the microscope they're going to come up with pretty similar numbers of blasts and so if you're above the threshold of 20 percent of the cells that they look at 20 percent of those are higher or the blasts, these immature cells. That defines acute leukemia. So, there's less ambiguity.

There are other things that can cause low blood counts. That's the point of the slide. I'm not going to go through in detail, but your doctor needs to be thinking about these and if appropriate in a particular situation exclude some other possible causes of having low blood counts. This just illustrates this murkiness of looking at these cells under the microscope. This is what bone marrow cells look like once we obtain them from the bone marrow with an aspirate and put them on a microscope slide and stain them and look at them under the microscope. We're looking for, again, these funny looking cells and on the left I'll just tell you that there were plenty of funny looking cells there and that turned out to be a patient with MDS. On the right even a well-trained pathologist is going to look at them and say, "Gosh, there are a bunch of funny looking cells there." I'm not pretending to… you may or may not recognize that it doesn't matter, but I'm just saying that one on the right is not normal and it has a lot of weird looking features that are pretty indistinguishable for MDS, but it turns out that patient did not have MDS. So, there are other things that can mimic MDS looking under the microscope. So, it's important to have well trained pair of eyes that are looking at these slides.

So, we make a diagnosis. There's some testing that's essential and then there's some testing that's not essential. I'm going to go through that. It's already clear based on what we said so far that an examination of a bone marrow specimen, a biopsy and an aspirate is essential. You cannot make the diagnosis of MDS, cannot do the classification, risk stratification without a sample of bone marrow. I'm often shocked when I give these talks how often I encounter folks who if I ask them to raise their hand how many of you have MDS and have never had a bone marrow aspirate. No hands should go up, but often they do. So, you cannot make the diagnosis, you cannot subtype it, you cannot say anything about prognosis without a bone marrow sample because, again, we need that material to look at these cells and to do some additional testing principally cytogenetics which we're going to talk about in some detail which has to be done on the bone marrow.

Q1: (inaudible 10:17)

Timothy Graubert, MD: So, what's an aspirate? So, we usually do two things at the same time both in the usually in the course of the same procedure from the pelvic bones. We get a biopsy which is a chunk, a biopsy of the material that gets preserved and looked at and then we use a syringe to use a vacuum and pull some of the liquid, the inner cellular contents of the bone marrow. That's the aspirate. So, it's usually done hand in hand and both are valuable.

So, these are things that must be done. We're going to get to this in a little bit. There are other things that are done in either a research setting or in sometimes in a clinical setting, but not standard of care. So, I'm just putting this up there. There are some other tests you'll see that are currently not part of the standard of care in terms of making a diagnosis, but some of these are coming. So, this illustrates what we were just talking about. This is the procedure that we're all familiar with and we love it. It shows the backside of the pelvic bone with the needle that has

gone through the skin, the subcutaneous fat, the cortex, the hard part of the bone and into the medulla, the spongy inner part of the bones and that needle is now in the bone marrow and then when the syringe is attached and we apply suction the liquid cells, the bone marrow where all of our blood, circulating blood, is formed come out to the needle and are collected and then put on slides and show on the right so we can stain them and look at that and, again, we're getting this material to look at them but also to collect cells to additional testing. I wanted to go into some of this additional testing a little bit of detail because it's important for everybody to know.

Q2: Do you often do the aspiration or you just do it in the beginning?

Timothy Graubert, MD: So, how often do you need to have a bone marrow aspirate? It's a good question. So, it must be done at the time of initial diagnosis to make the diagnosis to the subtype and then maybe that's the one and only time it's done or it's done later. Here are some of the scenarios why a subsequent marrow might be necessary. One is you're on a clinical trial and we'll talk about this and clinical trials often mandate or specify when you sign up to do it you say I agree that you can do a bone marrow biopsy six months into this treatment and three. So, there are landmark events. So, that's one scenario. Second scenario will be outside of a clinical trial just generally there's some change in your clinical picture and that's a more… it could be a significant change in the blood counts. Things were trucking along fine and then all of a sudden we start seeing some blasts showing up in the peripheral blood or the platelet count plummets. So, some change in the blood counts or something else is going on clinically. So ,generally speaking a change in the overall clinical condition where we're thinking okay, I better do a bone marrow biopsy because I want to see if my patient who was responding well to a drug have they lost their response and things are changing. So, I need to go back to the bone marrow and look at that. Has it evolved to acute leukemia? And so forth. So, it's usually outside of a clinical trial triggered by some change in clinical status and on a trial there'll be certain specific time points in that are (inaudible 14:01). Does that help? Okay.

So, I wanted to harp on cytogenetics a little bit because, again, this is standard of care today and everybody needs to be familiar with it and going to get into some territory that's more nuance. So, does this look familiar to everybody? This is a karyotype. So, sometimes hear both of those terms. Karyotype is what's shown here a picture of all the chromosomes from one cell. Cytogenetics is the test that we perform in order to get this result. So, you'll see 22 pairs of these long skinny lines. Those are individual chromosomes and pairs and an X and a Y. So, let's see where we are here in the room. Could this be from one of my cells or from one of your cells over there? What do you think? Could this be mine? Do we know? So, it comes down to these guys here that we all of us in the room have 22 pairs of chromosomes plus I have one X and one Y. That defines a male karyotype. It's not yours. And this is a normal karyotype. So, here's a different one. Now, two Xs no Y, but 22 pairs of other chromosomes. Is it mine? No. Could it be yours? Yeah. It's a normal… Well, this is a female karyotype. Is it normal? There's a clue on the slide there. There's a little arrow. See the arrow up there? Do you see what's going on here? Again, this is not easy. This takes experts, again, to review these things and call out these

findings, but you'll see nice aligned pairs of chromosomes everywhere except here, chromosome five, there's one. The other one is missing a chunk here. It's got a deletion. That's called Del 5Q, a deletion on the long arm of chromosome five, a very common recurrent genetic abnormality that we see patients with MDS.

Okay. Why am I torturing you with this? Again, it's cytogenetic testing to look at karyotype is an essential part of the management of every patient with MDS. It helps us make the diagnosis. If we see classic alternations like this and there could be stuff missing, entire chromosomes missing, bits of chromosomes that have broken off and rearranged themselves or part of nine connected to 22 and so forth and it gives us really valuable prognostic information. We know that particular patterns are associated with a better prognosis or a worse prognosis and it has implications for the therapy as we'll get to specifically this abnormality right here. I wanted to dig into this a little deeper. Now, we get into this is really Genetics 101. I'm sorry. We'll get off the subject in a minute if this is causing you pain, but I just wanted to give you a sense of where we're going as a field.

So, the genome is the instruction book that tells every one of our cells to do… to be a blood cell or be a brain cell or whatever. So, there's human genome. There's a copy of it in every one of our cells and you just look at the karyotype which is essentially the entire genome of one cell. If you imagine looking at those chromosomes with a microscope at a higher resolution you get down from the chromosomes to individual genes. We've got about 19,000 of those in the human genome and then if you had a microscope that zoomed even further now you're getting down to the individual letters within genes or basis as we call them, spell that here, ACPG. There are six billion of those in the human genome and so today we are, again, using this information for MDS patients at the higher level here we're looking at the chromosomes analogous to chapters in the book, but increasingly we're getting down to further resolution and we illustrate that here.

These are the tests that allow you to do that. So, we talked about karyotype looking at the big picture, the whole genome looking at individual chromosomes like chapters in a book. Has anybody had a molecular test for a gene called JAK2 or RUNX1 or FLT3? Do any of these ring a bell? Those are individual genes and, again, analogous to the words in the book and we are routinely testing for those. Those are absolutely essentially standard of care if you have acute leukemia, if you have other disorders. Right now not standard of care in MDS in the clinical setting, but that's what's been my single gene testing. We zoom into one specific word and say is there a mistake there or not? Panel testing means we can now look at a bunch of these concurrently instead of doing one by one. Exome sequencing means we're looking at all the words and then genome sequencing means we're looking at all of the letters in all the words, all six billion letters.

So, I'm putting this up there because, again, it's a spectrum and right now today we're at the top for MDS where karyotype is essential. That big picture look at the human genome is essential. The stuff at the bottom, four and five, for sure are entirely today in the research setting. In some

settings, some centers, our own, for example, we live right now we live at level three with MDS. We are routinely for 100 percent of our patients with MDS looking at 95 genes for mutations, but that middle area, again, and that's where the bar is moving and as you travel from center to center it's going to be different. Everybody should be at one. Nobody really today is a four or five. Most of the world is living somewhere between two and three. We are all moving towards five. This is the future. This is where we're going. Every patient with any kind of cancer is going to have their genome essentially characterized and we're going there, but it's years away and it's important across all of these domains to get this information.

I'm going to leave Genetics 101 if that's okay unless there are other questions and, again, we can talk at lunch.

Okay. You've made a diagnosis. Now, you need to subclassify. Again, that's a group of diseases. So, we need to know which bin to put you in. I'm not going to go through this in any detail. Maybe you can't even read this, but if you can you'll probably recognize on the left there are some of these terms that we've used. This is the World Health Organization classification of MDS to describe the different subtypes of MDS. This has evolved a little bit. A new revision of this system is just published. There are some nuance changes not a huge deal. It's not like we blew up the entire system and started over, but the point of this is just to say you'll start to see some new terms showing up. Are the old terms familiar? RAB1, refractory anemia? These are things that maybe some of you have heard about. So, the names will change a little bit but nothing of really any major consequence.

That's all I'm going to say about classification. Now, we're going to talk about prognosis or risk stratification and then we'll get onto therapy. I've made this point already. This is a syndrome. It's not one disease, it's many. We need to make the right diagnosis and subclassification and then we need to refine prognosis or define risk stratification. This is a question that every patient asks when they're newly diagnosed. How am I going to do? Because it's extremely variable. So, imagine you're on the top curve there. So, these are these Kaplan Meier curves that we all love as hematologist oncologists where it's just showing probability. So, one means certainty. So at the day of diagnosis everybody's alive. The probability of that is 100 percent and unfortunately these curves usually go down. So, the probability of being alive drops from certainty over time and the scale here is in years, a long time, a decade or more. So, this shows one prognostic system and I'll tell you a little bit more about that defines patients with MDS into five different groups. So, the group at the top, okay, if I'm 75 and you just diagnosed me with MDS and you tell me that based on some model I have a better than 50/50 chance of being alive 10 years later. I'm feeling okay about that. That's probably not that different than expectation if you were 75 and didn't have MDS. It's pretty… I'm feeling pretty good about that. Again, so that's really important to know because as your healthcare team we don't want to do worse than that. We don't want to intervene there and make the outcome worse than average 75 year old should expect, but if I'm on this curve. If I'm 40 and diagnosed with MDS and you tell me I have a less than 50/50 chance of being alive at two years, that's bad. That's not what a typical 40 year old

should expect and so, again, being able to kind of place a patient on one of these curves can help you begin to think okay, I need to be thinking about some aggressive type of therapy that's really going to shift the curve here and people up here do no harm. Don't cause problems that don't exist. It's an important thing to think about these if your doctor shows you curves like this and tells you you're in this category or you're in this category. This represents that average behavior of a large group of patients. These curves are drawn with 7,000 patients with MDS over time. You notice even in this best curve, patients are dying the first six months, but the frequency is slope here is much shallower. So, there are a lot of patients who are living more than 10 years, but even in these curves there are patients… a lot of patients dying early, but there are patients who are surviving a decade. So for an individual discussion with one patient in front of you, you have to be able to walk that line. This is what a population patients like me behaves, but I can't guarantee that even if you're on that good curve that where are you going to fall. Does that make sense?

How do we generate these curves? There are a number of different systems you hopefully have seen this one before, the IPSS, the International Prognostic Scoring System, widely used. Again, I'm not going to go into details, but the point here is to say that this useful tool because to put you in to use this instrument you only need information that is routinely available that every patient with MDS, this information should be collected. So essentially, your blood counts, those chromosomes, your cytogenetics and how many of the percentage of blast when we look at the bone marrow and we count a lot of cells, what percent of them are blasts. You only need those three things. If you're getting 100 percent of patients with MDS needs anyway and so we're not ask… you don't need anything special to be assigned an IPSS score and it stratifies patients very well. This was revised a couple years ago. So, most centers now are using this, the IPSS-R. Again, it uses exactly the same information, the same types of information – blood counts, blasts, cytogenetics, but now there's a little more granular detail and so it gets a little more complicated and there are five subtypes instead of four and so forth and even folks who think about MDS all the time can't keep this in their head, so thanks to the MDS Foundation there's a little tool you can go… there's a little calculator online or on your iPhone if you know blood counts, blasts, cytogenetics. You plug that in and it tells you what category you're in. So, it's very helpful.

Important points about the IPSS and, again, the curve I showed you a few slides ago was in fact this IPSS-R shown again on the left there. This really has been validated only at initial diagnosis. So, what's my prognosis at day one although it performs pretty well if applied later. It's six months after diagnosis or 12 months after Azacitidine or so forth, but it really strictly was only devised and validated at initial diagnosis and de novo, we talked about this a little bit. Some patients with MDS got it as a consequence of prior exposure to chemotherapy or radiation. Those are therapy related cases of MDS and those behave differently. You really cannot use this model for therapy related MDS. It's a few caveats there.

So, I put this in and I think we're okay on time, so I can talk about this for a minute. This is in part responding to one of the questions we got. If I'm diagnosed with MDS, can my brother

going to get it or are my kids going to get it? So, I want to talk about this subject a little bit which is stepping back a little bit and asking a slightly broader question here which captures the hereditary aspect – why did I get MDS? What causes that? Because, again, almost everybody I see asks this question. So as far as we know today, this really is a comprehensive list of possible routes to MDS. I just talked about this, these therapy related cases. We think between five to 10 percent of newly diagnosed cases with MSD today fall into this category of therapy related, prior radiation specific types of chemotherapy. When similar mechanisms, certain occupational exposures can do this as well. It's a little murkier, but Benzene and radiation outside of medical context they clearly damage bone marrow cells and can lead to MDS, but and very difficult to predict for an individual how much exposure really counts just pumping your gas or working in the petro chemical industry and bathing yourself in Benzene and so forth, but these… we know for sure that these are bone marrow toxins and can contribute to MDS.

So, there's this. Again, so far this is a minority of cases and antecedent disease meaning you had something earlier. So, aplastic anemia can evolve into MDS. There's an overlap, diseases like TNH can evolve into MDS and MDS can, of course, evolve to other things, but so there are certain patients who had a prior disease that predisposes them to getting MDS and then there's this which we're going to talk about in a second – inherited predisposition which exists, we don't know how important this is but it does… so basically the answer to the question was, yes, but… So, we'll talk about that now.

Aging in bold there… it's bolded to imply that as best we can tell most patients with MDS develop MDS by chance. It's a feature of living a good life, living a long life. So, that genome every time our bone marrow cells need to self-renew. We're not… The cells that we're born with cannot sustain us through a life, make blood for 80 or 90 years. Those cells have to copy themselves and self-renew throughout life. Every time they copy they're copying their entire genome, six billion letters, and they have to do it quickly. So, sometimes they make mistakes. Essentially every time we copy a cell we make mistakes. The vast majority of the time those mistakes are of no consequence we think because we got a big genome. There's a lot of room for error, but sometimes they don't. Sometimes they are of sequence and the thought here is that over time, over years, the accumulation of these random events by chance, the wrong things happen at the same place at the same time. So, aging or just chance is the explanation we think for most cases of MDS.

Am I losing you? You're okay so far?

So, let's talk for a minute about this inherited predisposition. It happens to be an interest of mine and, again, it's an area of active research and so there's much more that we will know about this, but here's a pedigree, a family tree, a family that I dealt with in St. Louis and you can't read this, but there's six individuals circled here who all were diagnosed with either MDS or AML or MDS that became acute leukemia, six, in close biological relatives. That's not chance. That's way above just the random possibility of these things (inaudible 32:04) in one family and this is

not the most extreme example I've seen. So, these families do exit and these diseases can run in families. We've known about this for years, rare syndromes that folks are born with that result in bone marrow failure, a bone marrow from early in life not producing enough bone marrow cells and those folks have a very high risk of developing MDS. If you weren't diagnosed with that in your genes or so forth, this is not how you got MDS, but this definitely occurs. So, this route of bone marrow failure to MDS and AML. We've known about this for a long time, but increasingly we're learning about other inherited disorders. This one was identified about 20 years ago, this one about three years ago, this in 2015 where an error, a mutation, inherited in one of these genes words predisposes to MDS or AML without that syndrome of bone marrow failure early in life. So, nothing until MDS typically earlier average patient is diagnosed at about 72. So, these folks are typically showing up in their 40s and younger. Collectively, this still accounts for a minority of cases of MDS. Hard for me to give you an absolute number because every study is biased in a certain way. So, we don't really know what the whole pie looks like and what sliver of the pie is accounted for by these inherited… but it's significant and the sense is that it's bigger than we think it is. So, that was my way of answering the question that came up, but this an active area of research. Most patients this does not apply to.

So, we're doing okay on time. We're about half way through and so I wanted to move to treatment if that's okay. We need to stretch? You guys have been quiet. I'm not hearing questions. You either are experts or you're bored. Go ahead.

Q3: My understanding is that this a relatively new disease. Can you maybe explain how did it pop up?

Timothy Graubert, MD: MDS?

Q3: Yeah.

Timothy Graubert, MD: Yeah. I don't think it's… It's not a new disease. We were actually having a conversation about this earlier. MDS has been around forever, but we didn't know it. I looked at my medical school book I was telling another patient here when I was learning about these diseases 30 years ago, almost to the day. My textbook didn't have anything in there about MDS, but that doesn't mean that the disease didn't exist. We just didn't recognize it, understand it, diagnose it. We didn't have terms 30 years ago. It wasn't captured in the databases. There's a database called SEER which is a national cancer registry database and MDS wasn't a diagnosis that was even included in SEER until about a decade ago and so I don't think it's a new disease. It's relatively newly recognized and still today underdiagnosed in many people's opinion and that's illustrated by the fact as you look to the papers and literature, this seems like a simple question. How many new cases of MDS are diagnosed every year? There's no agreement on that. The numbers out there are between 15,000 or so on the low end to as high as 60,000 – 65,000 on the high end. That illustrates the fact that we still have a lot to learn about the disease, recognizing and diagnosing and sometimes it's underdiagnosed. Somebody has anemia and it's

just not pursued. So, there's no evidence of the incidents since we've been diagnosing and capturing SEER the incidents. The new cases per year is flat or just relative of a decade timespan or so. So, it's not new, it's not increasing, but it's relatively newly recognized and appreciated.

Onto treatment. So, I'm going to go pretty rapidly through the general approach to MDS patients, how we think about therapy, what are the existing widely used therapies for MDS, really pretty quickly and then onto what's on the horizon. So, that's what the goal for the remaining 20 minutes or so, 25. So, we have three drugs shown there that are approved by the Federal Drug Administration for use specifically in patients with MDS, Azacitidine, Decitabine, Lenalidomide, and those are approved in a bust about a decade ago. So, new therapies really approved specifically for MDS in 10 years which is not acceptable and then we have a number of other agents listed at the bottom that are widely used for MDS standard of care. They just don't happen to be specifically indicated by the FDA for use in patients with MDS, but widely used.

So, here's the general approach to patients with MDS. You'll see kind of flowcharts like this in various flavors, but generally it begins at the top. Again, make the diagnosis which involves the testing that we talked about, subclassify patients and then really the first question you need to ask is are you symptomatic meaning are you perfectly fine? It's not interfering with your daily living or doing everything you need to do, your blood counts are okay. Then you move the right. Again, do no harm, observe. There's nothing wrong with doing and following folks for a while, but if you're symptomatic, you have overwhelming fatigue from anemia, you're getting infections, bleeding, needing a lot of transfusions to support those numbers. That's what I mean by symptomatic. Then we ask ourselves let's think about the therapy to see if we can intervene and make a difference in those symptoms. So, once you've decided this person is symptomatic and needs some therapy, generally speaking we will divide the population into two groups – the generally lower risk and the higher risk because the therapies are different generally in those areas. So, the next slide shows an expanded view that if you fall on the left, you're symptomatic and you're lower meaning in the old IPSS low Int 1 sort of in that territory in the new, the very good good or intermediate risk. That's kind of what we mean by low risk. Then you sort of fall down this decision tree and I'm going to touch on Lenalidomide. So, there's one vector that where you arrive to that drug. We're going to talk a little bit about growth factors. There's another arm that leads you there and then we'll get into HMA which stands for hypomethylating agent. Those are the drugs like Azacitidine and Decitabine or clinical trial. So, before I do that just the high risk arm. Again, it looks different here. The major decision is should we be thinking about a stem cell transplant or not and I'm going to talk about that in a second. Generally, that's not a first thing on our radar for patients with lower risk disease.

So, let's talk about first transfusion support, growth factors like Erythropoietin and drugs like that. Collectively, these are thing we refer to as supportive care meaning they're addressing symptoms, problems the patients have like anemia or low platelets and so forth, but by themselves they're not going to change the natural history of the disease. They're treating the underlying problem. They're not going to prevent progression, but they can address symptoms.

That's supportive care. So, a major part of that is transfusion support. We can't really transfuse white cells, granulocytes. That doesn't work, but we can transfuse blood on the left or platelets on the right and this is a mainstay of supportive care for most patients with MDS not without its issues as all of you know if you experienced this or caring for somebody who's experiencing this. On the red cell side there are allergic reactions, there are transfusion reactions, there's infectious disease that's largely been eliminated by appropriate testing. There's the accumulation of iron. This is a significant problem. So, these things come at some cost, but are mainstay. On the right, platelets. There, again, allergic reactions and then sensitizing the immune system. This is the major downfall of platelets. We tend to make antibodies to these foreign platelets coming into our body that rapidly clear those platelets from our body and the more you're transfused, the more antibodies you get the harder it is to find that a unit of platelets that's compatible for you and that will survive for a long period of time, allow immunization is a major problem that has not been solved from cytopenia and platelet transfusions.

Just a couple quick words on growth factors. It's hard to read the slide. I apologize, but they essentially come in three flavors corresponding to the three main lineages of blood, the red blood cells, the white blood cells, the platelets. The main one that's established in MDS is on the red cell side and these are drugs like Procrit, Aranesp are the commercial names. These are injections that support red cells. They are essentially providing pharmacologic doses of the normal hormone that our bodies make in the kidney and stimulate our bone marrow to make more red blood cells. That's what those red cell and growth factors do and they are very effective and widely used in MDS. I'll show you some data. In the middle are the white cell growth factors. Those are not routinely used in patients with MDS except in certain circumstances we can talk about that. On the bottom are the platelet flavor drugs not yet approved in MDS. We'll talk about this as well briefly, but on the near horizon I would say they will enter more general use.

So, just a quick word about the red cell support, the erythroid stimulating factors. I don't intend for you to be able to read all the details here, but the point of this slide is to say that there are tools that are available that do a pretty good job of predicting before you've received these drugs are you likely to respond or not and it essentially comes down to two things. One is do you need a lot of blood? Are you getting transfusions frequently? Or fewer transfusions? And the lower your transfusion burden the number of units you require, the more likely you are to respond to this drug and the second is we can measure that hormone in your blood, EPO, Erythropoietin. We can see how much your body is already making and if you're already making a lot you're unlikely to respond to getting more. That makes sense. Right? So, the combination of those two factors, your transfusion burden and the level of your EPO in the blood that goes into these models and you can see that in the best circumstances, low EPO level, low transfusion burden, you have about a 74 percent chance of responding meaning decreased transfusion burden or perhaps even transfusion independence with red cell growth stimulating factors and then it drops rapidly if you don't have those factors. So, that's useful.

That's all I'm going to say about growth factors really because, again, we can spend an hour on any one of these subjects.

Let me touch briefly on two other standard of care agents for MDS. First, is Lenalidomide, a drug that's had a significant impact in patients with MDS, an oral drug, well tolerated that has its major effect, again, on the red cell lineage improving anemia and especially in folks who had a karyotype like the one I showed you earlier missing a chunk of chromosome five. That's what on the slide here. So, in this large study and it's been replicated over and over again if you have this Del 5Q in your karyotype, you have a 60 or so chance of becoming transfusion independent taking Lenalidomide. So, that's huge. It's interesting that even if you don't have that, about a quarter of patients will have a response. We don't quite understand that. We now understand very well why these people do this, but it's not part of the labeled indication right now, but it's still widely used in this population and then these curves show that if you respond it tends to be pretty durable. So, over time these are as you move down here you're losing your benefit to Lenalidomide and it does go down kind of relentlessly, but the slope is relatively shallow. So, they're relatively durable. It's not a cure and eventually most patients will progress but it's had a huge impact. That's Lenalidomide.

Just a quick word on Azacitidine and Decitabine or Dacogen as largely similar sorts of activity in MDS, but I'm just going to focus on Aza because it's more widely used. So, Azacitidine, the most commonly used chemotherapy drug in patients with MDS, generally patients with higher risk disease. Patients do benefit from Azacitidine. They see improvements in their blood counts and this curve shows in a large prospective study over many years that actually they live a little bit longer. It's not a cure, again, by any means and it's not a gangbuster, but the folks who got Azacitidine you can see on the right side of the curve the natural history has been shifted and so on average the average living nine months longer than folks who didn't. So again, that's nowhere near where we need to be, but it's had an impact and widely used and, again, Decitabine hasn't shown the same survival benefit that has largely similar benefits overall.

I put this slide in just to summarize one other topic which is in the research setting many, many efforts have gone into saying okay Azacitidine is pretty good. How can we make it better? What can we add to Azacitidine to maybe improve the overall response rate a little bit and there have been dozens of trials testing Azacitidine plus X, your favorite drug, and I'll just say that they've all been disappointing. Nothing has been shown when in combination with Azacitidine to improve the response rate, survival, anything. This is one example of a drug (inaudible 47:52) study and big study and see that if anything that folks that got the combination they're on the left. They did a little bit worse than the folks who only got Azacitidine, but that's kind of a statistical thing. Essentially in most of these studies, the curves are basically overlapping. No difference. So, that's been frustrating and disappointing.

I just summarized probably a decade of work by hundreds of people and thousands of patients. So, we need to do more.

So, a word on transplant because, again, that was a subject of the questions that came in and, again, we can spend an hour talking about transplant, but let me briefly cover this important subject. Transplant, allogeneic transplant is the only therapy today that we know has the potential to cure this disease. However, fewer than 10 percent of the patients with MDS in this country, probably fewer than five percent receive an allogeneic transplant. So, we talked about it as a cure, but in fact it's a cure so far for a disappointingly small fraction of the patients and I'll get into the reasons for that. In a nutshell, if we're thinking about a transplant we have to match the donor and the recipient and so we do this called HLA typing. We look at family members, we look unrelated individuals and so forth. It's different than the blood type, PBL. So, you could be mismatched with respect to blood type, but matched with respect to tissue type or HLA and go through transplant. At a high level this is the procedure, which hopefully you've seen in some for before, but essentially a patient will receive some therapy, usually chemotherapy and/or radiation therapy. Stem cells are procured from the donor whether a family member or unrelated donor and then introduced into the recipient after they finished this conditioning, intravenously cells circulate homing to the bone marrow, repopulate and produce blood. That's a transplant.

We're going to get into who should get a transplant and why don't we transplant everybody. One of the major limiting factors for bone marrow transplant is this, this entity called graft versus host disease. This is because the cells although they're HLA matched, we hope, are not a perfect match unless they're coming from an identical twin and so once they get into the body can see the recipient cells and recognize them as foreign and start attacking them. So, that's the graft from the donor against the host. Graft versus host disease. This is still a major problem in the allogeneic transplant field. We've gotten much, much better at preventing it and treating it and recognizing it, but it's still rate limiting in many respects.

Generally speaking when we're thinking about whether or not a patient should be a candidate for transplant two main factors and, again, this is a complicated field, but there are generally two large categories of information we're thinking about. One is their prognosis. Again, imagine those folks up at the top. They're going to do pretty well if you leave them alone. I'm not going to transplant somebody with very low risk MDS. Period. So, whereas high risk MDS many years of life potentially lost. So, the first thing you think about is what risk category do they fall in and generally the higher risk patients we're going to be thinking about transplant. That's one. The second is it usually be strictly age. Now, we think about it more in terms of their biological age and I'll get into this in a second. The bottom line there is that there are 70 year olds probably in this room or certainly out there that can beat me in a 10K and they're biking every day and doing great and there are 40 year olds who can't get out of a chair. So, age is not a robust indicator of how somebody's going to do in a transplant. So, we really look at their biological age. The age plus does their liver not work? Do they have heart disease? Do they have lung disease? Diabetes? Other things. So again, as we've moved away from age as a strict criterion to more this entity I'll call the comorbidity index comes up in a second. Those are the two general categories of

information worth thinking about at the get go. Do you have high risk disease and do you have a comorbid picture that suggests that you could tolerate a transplant.

So, that type of information has been used a number of ways. Here's one computational model that essentially looked back at a large group of patients who were transplanted and integrated all that information and there are two curves here. The higher risk patients are here in blue, the lower risk patients are in this orangey color and what it's showing is that there's a point of time at which these curves cross and beyond that the patients with the higher risk disease ultimately have a better survival. This survival looks terrible here, but ignore that for the time being. The point is it's better for the high risk disease whereas earlier on the higher risk disease are patients are falling more rapidly. So, it's a complicated way of showing that, again, higher risk patients tend to stand to benefit from a transplant more than lower risk patients, but there's a price to pay early and there's a crossover point that you have to get beyond before you can really realize that benefit.

Maybe I can answer questions if that didn't make sense.

Here's an illustration that's comorbidity index. Again, this is now looking… everybody's treated the same way adjusted for all other things that are confounders and just ask the question at the day of the transplant were you fit? Did you have a low comorbidity index? Those are up here. Or did you have increasing numbers of these other factors, again, like heart disease, lung disease, etc.? So, that kind of information above and beyond strictly age is a nice tool that can help you stratify. I'd be worried about sending a lot of patients in this group to transplant whereas I'd feel pretty good about that.

So, prognostic factor and comorbidity are key parts of the discussion about transplant.

In the remaining minutes I wanted to talk about research. We have just a couple minutes left. Are we okay? Bear with me for a few more minutes about clinical trials and what's on the horizon. This is really, really important. I've shown you here on this slide just some of the jargon to make sure everybody is familiar with this. Different types of trials because you'll hear about this. The stuff on the left is basically laboratory research which has to happen to get into clinical research. So, no drug gets approved/used in patients until clinical trials are done in patients and this doesn't happen until much laboratory research happens first, but we're going to focus here and just make sure you guys are familiar with these terms especially in phase one, phase two, phase three because, again, these bantered about. Phase one is basically there's going to be one group of patients receiving a therapy. Everybody gets the same thing and we're trying to find out is this safe? Can folks tolerate it? Are there side effects or is there an acceptable toxicity? That's the goal of a phase one study and that needs to be done generally before a phase two and now we're asking really does this new intervention that we're doing have activity? Do we see some signs that actually it may be working? And you'll define that up front. Working means, again, it could be fewer transfusions, living longer, etc. You build that in. You design that. So, we're looking

for a signal for efficacy here. Phase three trials are the big randomized trials where folks through a coin toss get a standard treatment versus the new treatment that's already been shown to have some activity in a phase two trial and now we're really comparing them head to head in a controlled fashion. Say is it really better than standard of care. That's phase three. Phase four happens generally later to see if there are… if this translates into the real world outside of these contrived experimental academic centers. Are there rare things that happen? Are there things that happen late after there's been more years of observation? Most trials are in the phase one, phase two that you're likely to encounter in an academic center and these are essential. This is the only way we make progress. If we don't do these clinical trials I'll be here 10 years from now talking about Azacitidine and Lenalidomide. The only way we're going to make progress is if patients are courageous and gracious enough to consider these possibilities, go through the discussions and sign up and participate in these trials. Fewer than 10 percent of patients with any cancer diagnosis in the US ever go on a clinical trial, far few of those, usually single digit less than five percent and for a disease like MDS whereas you all know our current therapies are not acceptable we have to do much better than that. So, clinical trials are essential and there are a lot going on.

I am going to have to make some choices here. So, let me… there are three clinical trials that I was going to illustrate. I actually think I'm not going to do justice to any of them. I'm going to save those for questions.

Let me go right to this slide which you cannot read, but the point of this is to say that I probably should have said this at the onset. In my opinion, take this with a grain of salt, every patient with MDS in the United States should be seen in an academic medical center or a cancer center that has a team of healthcare professionals, researchers, doctors, nurses, experienced in the care of patients with MDS. It's a rare enough disease compared to breast cancer, lung cancer that in the community your doctor has seen a few cases of MDS a year. It's hard to be on top of everything. I'm not saying that all patients with MDS should receive all of their care in an academic center, but at least once they should. I'm on a soapbox here I realize. I'm sorry, but you've given me the microphone. To at least be sure we agree with the diagnosis because as I alluded to there can be some uncertainty. Do we agree with the initial treatment plan that your local doctor has proposed and maybe that's it and you go back and all of your care is managed by a community or a community hospital or private practice, whatever. That's fine or you have a collaboration now. You have an expert who can be a resource to your local doctor to answer questions and give advice or you're a candidate for a clinical trial and it's feasible, practical for you to receive care in a center and participate in a clinical trial. So, it could play out in many different ways, but I strongly feel that this is a disease where an experienced MDS team and an academic medical center needs to interact with all patients at some point in their journey.

So, at our center and we are a consortium between Mass General, Dana-Farber, BI, Beth Israel Deaconess, this is the Harvard Cancer Center. We collaborate. We exchange ideas. We generally share the same clinical trial portfolio. The studies open at one center will be open at the other

center and vice versa. This is just a portfolio of clinical trials currently open at our cancer center for patients with MDS and, again, you can't read that, but I hope you see that we have a pretty robust portfolio of clinical trials and we try at all times to have clinical trials available for patients at all stages of their disease – never been treated, low risk, high risk, previously treated with Azacitidine and Procrit, etc. We want a clinical trial for every unmet need in this population and we have a great team in Mass General. I've listed the doctors on the left. I've highlighted Andy Brunner who's joining our team this summer and will specifically focus on MDS only. He'll see other patients but he will be our MDS expert and I hope in the future Andy's here that you'll be hearing from Andy and we have a great group of colleagues in our bone marrow transplant center as well that we collaborate with.

Okay. I'm going to stop there and see if there are any other questions. Don't hesitate to reach out if things come up later. Thanks so much for your attention. Any questions at this point?

(Applause)

Questions or should we move on? Let's see if there are any questions.

Q4: I have a question. Can you just clarify the blasts again?

Timothy Graubert, MD: Yeah. So, blasts are short for myeloblast. That's the name of the cell, the white blood cell and it's a primitive one. So, cells go through this stage of maturation. They're born in the bone marrow and they grow up a little bit and then they exit the bone marrow and go out to the blood. The white blood cells by the time they go out to the blood should be beyond that stage of myeloblasts. That's an immature cell. That should only be seen in the bone marrow and should not be in the blood in most circumstances and so what we're doing, again, is looking at those stained slides under the microscope. We're counting up all of the cells and assigning a percentage to all the different types that we can identify and they're usually 20 or 28 different categories that we're counting up and usually count 200 or 500 cells in a normal bone marrow the blast count, the myeloblast count should be less than five percent of those cells, less than five percent. As I told you if it's above 20 percent in either the bone marrow or the blood, it should be zero in the blood, but if it's 20 percent in either that's acute leukemia. Anywhere between so with MDS you can have a blast count of zero. So, you don't have to have elevated blasts to have a diagnosis of MDS. So, low risk patients often have a normal zero to five percent blast count, but anywhere in that five to 20 percent is already abnormal and patients with MDS typically have blast counts in that range, but it can be normal. Does that make sense?

Q5: I'm on Vidaza and the Vidaza is helping. So, I understand it doesn't cure it, but does the person stay stable or is the disease still progressing?

Timothy Graubert, MD: It's a great question and I hope everybody heard and this is commonly asked. So if I'm on Azacitidine or Vidaza, the same thing, and I'm doing okay, tolerating side

effects, issues and benefitting, let's say, first of all how long should I take it? Should I stay on it? That's not exactly what you asked, but the answer to that is as long as you're still in that category tolerating it okay and deriving some benefit and we have patients who are getting it monthly for years, a year, two years, etc. So, that's the first part of the answer to your question. As long as it's going well and patients are benefiting the recommendation is that we do not stop. Let's stop and see how things go. No, it's we stop. What you're really asking is okay, I'm on month nine, month 10, things are going well, but what's going on? Is it really reversing what's going on underneath and a lot more work needs to be done. I would say superficially yes the disease continues to evolve and change despite even in that optimal circumstance where you're tolerating it well and the blood counts are improving, you're feeling better. Even in that setting the disease is still not static and this is probably why in part patients will really inevitably lose their response, become refractor or resistant to drugs like Azacitidine or never responding in the first place.

Q6: Can you give us some sense for how you classify the frequency of blood transfusions? What is a lot and what is normal and what is range?

Timothy Graubert, MD: That's a great question. It's kind of murky in the field. Outside of a clinical trial it's there I can't give you a there's no standard guidelines for categorizing numbers of transfusions and so forth and what we should care about generally it's in a setting in a clinical trial where we're trying to impact that reduce the transfusion burden and there will be an arbitrary definition. Four units in the last month, a transfusion every month for the prior six months, something like that that's usually an entry criterion you have to satisfy to get on a clinical trial. We do know that outside of a clinical trial that the more you've been transfused, the more you accumulate iron that that has an impact on survival. Heavily transfused patients, patients who accumulate iron have an inferior survival compared to patients who don't. Now, there's still controversy because the heavily transfused patients who accumulate iron are the patients… they tend to be patients who have higher risk disease anyway and so is it really the iron in the transfusions themselves or is that just a proxy for having more aggressive disease. We haven't resolved that yet, but it's clear that high transfusion burden and iron overload reduces survival and in retrospective studies removing iron seems to improve that, but it has not yet been shown in a prospective fashion that that's the case. There are ongoing trials to look at that.

Q7: Is there anything that we can do in terms of improving our daily lifestyle and habits and I don't mean to sound funny here, but my hematologist warned me about drinking beer and said very adamantly I could have one beer a month and coming from Milwaukee, a beer town, I thought that was a little ridiculous.

Timothy Graubert, MD: I think that's a great segue for Joan's talk because Joan is going to talk about your lifestyle, I think. Generally, what can you do in terms of diet and exposure to other things to have the best possible quality of life and quantity of life? So, I'm going to turn that to you if that's okay.

Thanks again and I'll be around if there are other questions.

Jean Ridgeway: Meander back to our seats and we'll get going with the rest of the morning and the afternoon. Sound good? We'll continue to talk.

So, good late morning to everybody. My name is Jean Ridgeway and I'm a nurse practitioner and I'm here on loan from the University of Chicago. So, I arrived last night at midnight. I feel a little discombobulated, but that's okay and I'd like to welcome all of you and thank you for taking time out of your busy schedule. It's a gorgeous day outside here. We are inside, but that's okay.

What I'd like to do is really get a little bit more involvement and so I like to start off the session by giving you a snapshot of who I am. I have slides that will discuss that stuff, but I would think most of you came today because you either have a question, are a patient or are a support person, a caregiver and so what I'd like to do is go around the room and give you the opportunity to take the mic. Remember, you got to push the button in order to activate the sound system so that I can hear you and that the other folks who are here can hear you, but if you want to just give us your name, let me know where you're from. I don't know the East Coast. I just found out that Maine is an hour and a half away. It's too bad I don't have time to go visit, but just give us a little snapshot of yourself if you're the patient, if you're the caregiver, if you're a family member and if there's something that you were hoping to understand today, have the opportunity to ask a question today why don't you let us know that? I have a couple rules about participation. You cannot bash your doctors or healthcare team. That's a no-no. We're not going to do that today. Healthcare is a commodity and we can talk about getting second opinions, but let's not drop names or doctor bash. I think that's fair and then as you share your little story, let's keep it to an elevator speech, not a filibuster. I know I'm on the East Coast, but I think will help us expedite and go around.

Lunch is going to be brought into this room at about quarter till. We'll leave those folks alone. They're going to set it up in the back and I leave it up to you whether you want to sit and chat with one another or if you want to have a working lunch and we'll kind of go through things, but hopefully my role with this is a facilitator. I'm not here to ask the questions. I'm here to help hopefully you understand a situation in your life or a loved one's life and as we go around the room, I have one other question. If you weren't here what would you be doing?

So, I'm going to give you a little history of myself. I've been an oncology nurse for a long time. I've spent 30 years in malignant hematology. I'm very interested in Myelodysplastic Syndrome. My career looks at somebody who stayed at academic centers. So, I was at the University of Illinois for 15 years and my physician program and myself migrated to the University of Chicago which doubled my commute. I live in the City of Chicago which is 35 miles in length from north to south. I work in the south. I live in the north. So, I enjoy books on tape when I commute and I

have a special interest in Myelodysplastic Syndrome. I have a Master's degree in oncology and nursing as well as a Master's in genetics. So, what our physician friend was talking about is very familiar to me and I work as an outpatient nurse practitioner with folks who have Myelodysplastic Syndrome or leukemia and are having stem cell transplant. My special area of interest is older patients with MDS heading towards transplant. So, those folks who are 65 or 70 and above going to allogenic stem cell transplant and that was my area of doctoral research and so we have a special niche. If I wasn't here today I'd be bike riding. I love to cycle. So, I cycle on the road. I have many broken bones to show it. So, that's where I'd be if I wasn't here today.

So, I'm going to start with my left. If you'd introduce yourself, give us your first name, where you're from and a little snippet about what are you doing here.

Q8: Morning. My name's (Attendee). We're here as support for my father-in-law, (Attendee). We've a very large support group here this morning. I think we're all here to gain more information overall.

Jean Ridgeway: Where would you be if you weren't here?

Q8: I'd be clamming.

Jean Ridgeway: Clamming! We don't do that in the Midwest.

Q9: And I'm (Attendee), his wife and I'd be clamming with him.

Jean Ridgeway: Okay and you're here with… is this your father?

Q9: My dad.

Jean Ridgeway: Your dad. Okay. Next.

Q10: My name is (Attendee). They call me (Attendee).

Jean Ridgeway: Why is that?

Q10: A nickname.

Jean Ridgeway: Okay.

Q10: From my grandmother years ago.

Jean Ridgeway: Very good and you're here as the patient? Do you mind answering when were you diagnosed with your MDS?

Q10: (inaudible 1:14:09).

Jean Ridgeway: Okay. So sorry. Where would you be if you weren't here? What would you be doing on a nice sunny lovely day in Boston?

Q10: (inaudible 1:14:24) outside.

Jean Ridgeway: Drinking outside. Okay.

Q10: Having a few beers.

Jean Ridgeway: Very good. (Attendee)'s next.

Q11: I'm his wife, (Attendee), his caregiver. He's hard of hearing, so that's why he hands everything over to me. He's had MDS since a year ago May we found out and he was on Azacitidine and through December.

Jean Ridgeway: Can you all hear her?

Q11: I thought you could hear me. He was on Azacitidine through December and he developed an infection and was in the hospital a few weeks and they gave him blood, but his blood's okay. Everything's good except they have not started the chemo back. We're waiting for that. And what would I be doing? The same. He'd probably be clamming and we'd be watching them.

Jean Ridgeway: You'll have to fill me in over lunch how to do that. I have visions of a sand pail and a bucket, but that's probably not correct.

Q11: He's the expert.

Q12: Hi. I'm (Attendee). That's my dad. We're here to learn more about it and support and I'd probably be working if I wasn't here.

Jean Ridgeway: And are you all from the Boston area?

Q11: Metro West.

Jean Ridgeway: Metro West.

Q12: Central.

Q13: I'm (Attendee). I'm his wife. That's my father-in-law. Just here for support and I'd probably be working in the yard.

Jean Ridgeway: Working in the yard. Very good. You do have a big group here. We're all feeling a bit outnumbered. Nine. Okay.

Q14: Hi. I'm his daughter, (Attendee). I'm here for the same reason everybody else is for my dad's support and to learn more about MDS.

Jean Ridgeway: And what would you be doing?

Q14: I'd be working all weekend.

Q15: And I'm his daughter, (Attendee). I'm here for the same reason to learn a little bit more about it and what his options could be in the future and what his future lies for him and if I wasn't here, I'd probably be out golfing.

Jean Ridgeway: Very good. You have your own microphone down there.

Q16: And yes, I am the last of the support group. I'm number seven, I believe. My name's (Attendee) and I am (Attendee)'s husband and (Attendee)'s son-in-law. I'd be the caddy on the golf course. So, but we're here to support (Attendee), obviously, and to learn more and be a better part of the life going forward.

Jean Ridgeway: Great. Thanks. I think in my experience of having family members go through treatment as well as sitting on the other side of the chair and being the care provider support systems and caregivers are essential to care and success and it's great to see that you have so many people here. Good for you. Thank you all for coming.

We know who you are, but what would you be doing if you weren't here?

Q17: (inaudible 1:17:38)

Jean Ridgeway: Working in the lab. Okay.

Q18: Hi. My name's (Attendee). I have a grandfather with MDS. So, I'm learning some more information and if I wasn't here I'd be golfing. So, I'll join the group.

Jean Ridgeway: Very good. Is your grandpa local or…?

Q18: Yes, down in Southern Worcester County, Mass. So, lower Mass.

Jean Ridgeway: Very good. Well, thanks for coming. And I hope… I know that at your places where you're sitting that there's a booklet called *The Building Blocks of Hope*. So, there's lots of great information in there. Oftentimes extras are brought. If you'd like to bring additional ones home it's that whole three ring binder. I think Tracy, do we have extra ones out there?

Tracy Iraca: We don't have any extras today but we can always send it to you.

Jean Ridgeway: They'll send it to you. It's also available online in a PDF format so you can download it and print it, etc. So, it's there. Next.

Q19: My name is (Attendee) and I'm a patient with MDS and I was diagnosed three years ago and I'm from Canton, Connecticut which is west of Hartford. If I wasn't here I'd be nurturing my roses and out walking.

Jean Ridgeway: Enjoying life. Very good.

Q20: Hi. My name is (Attendee). I'm from Pomfret Center, Connecticut and my mother was diagnosed with MDS a couple months ago…

Q21: No. Weeks. A couple weeks ago.

Q20: It felt like months.

Jean Ridgeway: And you're here to learn more about it?

Q20: Yes.

Jean Ridgeway: If you weren't here where would you be?

Q20: I might be golfing.

Jean Ridgeway: He might be golfing. Very good.

Q21: Hi. I'm (Attendee). I'm (Attendee)'s sister. We're here for our mother, (Attendee), who was diagnosed just a few weeks ago. She is in the high risk category and has just completed her first seven days of injections. So, we want to learn as much as we can.

Jean Ridgeway: And that probably would be Azacitidine? Seven days.

Q21: Vidaza.

Jean Ridgeway: Is your mom here today or no?

Q21: No, she is still extremely weak. I don't know how long it's going to take to see any big improvement, but…

Jean Ridgeway: Anybody want to address that? Anybody else who has gotten treatment want to talk about the fatigue and… Go ahead. Feel free.

Q22: I was diagnosed in September and have been on the Vidaza since February and I have noticed over the last several months I really feel much better. I don't take naps anymore. I'm just very energetic.

Jean Ridgeway: Would you say that the improvement was gradual?

Q22: Yeah. It was gradual. I mean, you didn't notice it, but I just find…

Q23: It took a few months because first the counts go down before they go up. It took a few months, but he's doing great.

Q21: Thanks. That's great to hear.

Jean Ridgeway: Good. Thanks. You're next.

Q24: My name is (Attendee) and I'm a caregiver with (Attendee). He was diagnosed September and what would I be doing? I'd be out in my garden.

Q25: There's nothing more for me to say.

Q24: Go ahead.

Q25: Good morning. My name is (Attendee). I was diagnosed as my colleague down back in September. So, I'm basically here to learn more about what's going on with my body and my problems and if I wasn't here I'd be repairing my front door right now with some help from Home Depot. Thank you.

Jean Ridgeway: Very good.

Q26: So, my name is (Attendee). I actually do MDS research. My research is patient focused research. So, I'm here to learn from all of the experts around the table, the patients and the caregivers.

Jean Ridgeway: What are you looking at?

Q26: So, I work at Cicada and we do clinical trial research, but my work is focused more on bringing the patient voice to what we do and developing patient reported outcomes so that we capture the most relevant aspects that are important to patients and their care.

Jean Ridgeway: Very good. Welcome. So, what she's saying is that besides just medication and what does it do and the data that gets generated and the slides that you saw with graph, the other side of medicine is what is it like with boots on the ground? What's the lived experience? What are things that you're feeling, experiencing that perhaps you may think that you're the only person like your mom still being fatigued not knowing if things are normal or abnormal, just trying to get an essence of what are patients really… what are they living with and how can perhaps we better understand it.

Q26: Yeah. So, I care most about how you're feeling, how you're functioning and how that impacts your day to day life.

Jean Ridgeway: Okay. Very good. So if you have something to say, catch (Attendee) at lunch.

Q27: Hi. I'm (Attendee) from Natick, Mass and I work for a consultant for Genoptix Medical Laboratory which is owned by Novartis and we do genetic testing. If I wasn't here I'd be running.

Jean Ridgeway: Very good.

Q28: Hi. My name is (Attendee) and I'd like to… First of all, I've had this… it was over 24 years ago that I got this and it took over two years to diagnose and I've been treated for 21 years. I'll start 22 years in about a month and a half.

Jean Ridgeway: Do you want to share your story a little bit? I mean, that's a long time. Help us understand what's going on a little bit.

Q28: I really applaud all of you here because especially this group over here. You have to be your own advocate when you have a rare disease for the general diseases that are out there you have a lot of support and a lot of expertise. When you get into this area it's not as doctor Graubert said they only really realized in the medical industry started dealing with this about 25 years ago. There was nothing before. There were very rare things, but they didn't teach it and there weren't centers other than the Fred Hodgson Institute back when they lost Carl Sagan back in about '76 or '96, but I just want all of you to know that if you follow and find doctors who will help work with you not just go, "Oh, okay. Here. We'll just give you this." You need to work in concert with them and you'll have a very good survival potential and I want everyone here to know I've been through clinical trial set NIH in Bethesda, Maryland National Institute of Health and I sought out treatment. I worked with foundations like this foundation and you have to educate yourself because there's not the expertise out there and you're not going to find that

many other people to communicate with when you have questions. I've been on lists for a long time where I used to communicate. In fact, my doctor used to laugh at me because I used what he called a chat room back before we really had the Internet as we know it now where you can search. There are wonderful things that can be done out there and I want people to realize no matter what age you're at you have the potential to have a long survival. I've had over 438 transfusions of packed red cells and 32 of platelets just to survive low points and I went for almost 13 years on another drug that I chose that they won't allow me to have anymore and I was totally transfusion independent for all that time with high counts. Now, I'm living with low counts and they're amazed because when they had the big snow in Gloucester last year when I met (Attendee), they had over about 130 inches. The snow storm where they had 44 inches, I was out shoveling snow and I had hemoglobin between 6.9 and 7.7 and I shoveled snow and I didn't breathe hard because you just have to pace yourself but keep pedaling the bike and you won't fall over.

Jean Ridgeway: Thanks.

Q29: I'm (Attendee) and I'm very proud of (Attendee) and I can't keep up with him.

Jean Ridgeway: You had a question. Go ahead.

Q28: You had a question.

Q30: You don't have to share this, but I'd like to know if you're high or low risk.

Q28: I am high risk according to NIH. I don't agree with them. I am being treated by Dr. Fathee (sp? 1:27:09) who is one of Dr. Graubert's staff and he's a very impressive man and he's doing research as well. Again, you have to have an energy with the people who support you. I have nurses who gave me transfusions 20 years ago that I've still been dealing with now until I moved to this area. I was in Upstate New York and I've gone to medical conferences starting in 1996 out in San Diego or Philadelphia. San Diego was the following year and I've been involved with people that would impress you so incredibly. There was one woman at the conference in San Diego in '97. Her daughter, her platelets went to zero twice while she was at the conference. She was at MD Anderson in Texas. She graduated high school a year ago. So, no matter how low the points are as long as you keep pedaling that bike, you don't fall over. That's the secret. Thank you.

Jean Ridgeway: Thank you. What would you be doing if you weren't here?

Q28: I'd like to be playing golf, but I smashed my elbow severely and I have to have another surgery coming up soon because they can't straighten my arm enough, but I'd probably like to be playing golf, most likely would be mowing the lawn or sneaking off to the festival in Gloucester where I live now because they have a wonderful festival right now. In fact, I'm going back for

the second day of the Greasy Pole contest. They have a 30 foot telephone pole horizontal and put grease on. You have to walk on it and get the flag.

Jean Ridgeway: Are you a participant?

Q28: I'm not a participant. Yet. But some people are quite incredible and yesterday it took them around two hours and went through all these people over and over, but there have been some times where the guy will win Friday, Saturday and Sunday.

Jean Ridgeway: What's the prize? Like a mug of beer?

Q28: I don't even know other than the title. One of the things is so if you win on Friday you're always qualified to go in the event on Saturday. On Sunday, it's only past champions or people who were invited.

Jean Ridgeway: Very good.

Q31: (Attendee), I'm over here. If you fall off the pole what do you land in?

Q28: Water.

Q31: Water.

Q28: It's right off the beach at the hotel. They're out probably a few hundred yards and they're up on this big platform. They're about three meters or 15 feet off the… or five meters off the water and they come out in costumes yesterday for the first round and then they get more serious, but it's quite the thing because as you get out on the pole it starts springing as well. It's an interesting thing to watch. Some of the people are quite incredible. I'll let things go forward here. Thank you.

Jean Ridgeway: (Attendee)?

Q32: Hi. I'm (Attendee). I'm from the North Shore. My mom, she was diagnosed at about a year and a half ago with MDS and she lives on the Jersey Shore. So, I go down there once a month to go to treatment with her and just trying to find out what more I can do to help her.

Jean Ridgeway: Where would you do?

Q32: I'd be at the beach.

Jean Ridgeway: At the beach.

Q32: Yeah.

Q33: Hello again. This is (Attendee) and I think you can appreciate this in that I grew up in Milwaukee and went to the University of Wisconsin. So, my beer question is very serious.

Jean Ridgeway: Valid. Very valid.

Q33: (Attendee) is interested, but I'm really not being facetious because I would be interested in how will this affect us in our daily lives. Like for example, my hematologist didn't want me cutting the lawn because she was concerned that I would get some kind of infection from the mold in the ground and we actually cancelled a cross country trip because of her not wanting me to be in an airplane and I'm just wondering what are the boundaries? Do I have a hyper sensitive hematologist or is this norm?

Jean Ridgeway: Well, it's not a simple answer in that everyone is different. Some people in this room have a low white count that may presuppose them to infections easier. Other people may only be anemic and so it's you cannot make a generalizable suggestion for everyone, but her concern is that I don't know your blood counts and I don't know your history. So, that's part of the answer to the question is I don't know what pre… I just don't know what's going on in your healthcare, so I would say I'll speak to you like people at our institution. If they have a very low white count, we make the same suggestions. Be careful with having someone else cut the grass because you can aerosolize this fungus, which if you have a low white count and a compromised immune system you may… you could get bad lung infection that they're different to treat and it could be life threating. Now, (Attendee). I don't know what (Attendee)'s blood counts are. He's obviously out there cutting the grass. So…

Q28: Very low.

Jean Ridgeway: Very low.

Q28: (inaudible 1:33:10).

Jean Ridgeway: But I will tell you there are guidelines and suggestions. Some of my patients will get kind of heavy duty masks and one of my guys sent me a picture with like an air mask on the kind of like for an air raid with a great big chainsaw in his hand as he was chopping down wood because that's how he heats his house. So, he's fine. He's been doing well. Can I say with certainty that that would be absolutely true? No. So, it really is a balance. As far as airplane travel, it can be difficult. You just don't have any control over the folks who are sitting in front of you, behind you, side of you. They say one of the dirtiest places is the seatbelt that we put on. So, and then it's recirculated air. So, I don't know what your counts are. What we suggest if somebody is relatively cytopenic is if they can drive, it's better. It's safer. You have more control over everything than flying. You may do great. You may fly out. I had a patient fly out to her

nieces wedding in Arizona and ended up in the MICU about 10 days later. She extended her vacation because it took about a week for whatever viral illness that she was exposed to more than likely either at the airport or on the airplanes affect her. So, when you see the spectrum of possibilities, I think providers get much more cautious when they… We look at numbers and it's terrible. Providers look at numbers and make these very broad statements of suggestions, but they are suggestions usually backed in good common sense and data, but your physician is not the warden and you don't have any chains on. So, I would suggest you do some type of moderation. The beer thing. Do you want me to address the beer thing? Okay. Let's address the beer thing. I don't know what other medicines you're on. Moderation is always good. A glass of beer a week, how big is a glass? You're doing a 64 ounce stein, I'm not really sure. So now, I ask how big the glass is. So, that's… pardon? (Attendee)'s shaking his head.

Q28: (inaudible 1:35:40).

Jean Ridgeway: Once a month.

Q28: (inaudible 1:35:43).

Jean Ridgeway: It seems pretty extreme. It seems pretty extreme. A glass a week, a glass every couple of days. Just be careful. I don't know what the other medicines you're on. Some medicines can affect your liver with that as well. (Attendee).

Q34: I'm (Attendee)'s wife and I would say as a caregiver and witness it's also difficult and I feel for people who are here with grandparents and parents and so forth dealing with this because of the kind of issues we're talking about. A lot of this is the grey area and it's easy in some ways, not fun, but when the person's really not feeling well then it's hard to watch that person not feeling well but then the person wants to lie down and you don't have to worry about it. When the person's feeling better and you still know the person has the condition it gets a little bit more complicated. So, I think these are really issues with the person talking about patient care and so forth to think about both for the patient and for the spouse or caregiver. It's like I have seen (Attendee) outside gardening when his numbers were low and he had been in the hospital having picked up a virus because his numbers were low and it's like I don't want to tell him to stop living his life, but his doctor was not coming from left field. So, I think some of these things are very complex and it's good to be with people who are considering all these issues.

Jean Ridgeway: Where would you be, (Attendee), if you weren't here?

Q34: Outside somewhere.

Jean Ridgeway: (Attendee) would be outside somewhere. I'm with (Attendee). (Attendee)?

Q35: My name is (Attendee) and we come from Stafford Springs, Connecticut and I am the patient and I have those diagnosed in 2012. More so I went to the Mayo Clinic because I had a condition of a terrible itch now for 10 years and no one can seem to discover what was the problem. So, I went to the Mayo and they found another problem, but they didn't find the reason why I was itching. I'd be interested if anyone who has this condition has an itch, a terrible itch, and also I'm being seen by several hematologists. I have one in Florida. I have one in Hartford and I'm going to have one on Cape Cod soon. So, if I wasn't here today, well we're going to my daughters in Wayland and then we're going to finish cleaning out their cellar. That's what we'd be doing.

Jean Ridgeway: Anybody here with MDS have problems with skin itching? Skin itching?

Q36: (inaudible 1:38:44) lotion head to toe.

Jean Ridgeway: What do you use? What kind of lotion?

Q36: I use a combination (inaudible 1:38:57)…

Jean Ridgeway: Will you do the microphone for us?

Q36: I use Vaseline Intensive Care during the night when it happens. It doesn't happen all the time and sometimes three or four times a day and sometimes none and we can't pinpoint it. It's nothing he's doing. It's nothing he's eating. It just happen and there's no answer to it, but the lotion helps a lot.

Q35: After seeing I don't know how many different doctors trying to diagnose this itch, I'm the only one I bet was on kind of all kinds of antihistamines, lotions, Prednisone and the only thing that really helps with the itch for medication is something I find Chlortabs which is like Chlor-Trimeton and when it's bad I have to take it every four hours, but like that it comes and goes. It fluctuates and I do have lotion all over the house that I keep putting on.

Q36: He had it on his chin and I used the cortisone with aloe in it and that stopped itching.

Q35: Sometimes it's worse like at the beginning of this week it was terrible. I was going crazy with it, but I mean 10 years is a long time.

Jean Ridgeway: Ten years is a long time. Honestly, I've done these forums for a number of years never heard anybody talk about itching. So, that's news to me. Do you have anything about itch?

Timothy Graubert, MD: Nope. No magic secret, but it's not that surprising to hear about this symptom not strictly speaking with MDS the medical term we use is pruritus. It just means

itching. Pruritus is very common in a related group of disorders called myeloproliferative neoplasm, MPN, diseases like polycythemia vera. So, itching can be the first manifestation and can lead to a diagnosis of P-vera and there is just like there's an overlap between aplastic anemia and MDS where some patients live in the middle or move from one to the other there's an overlap between MDS and MPN. That's actually formally we call it MDS-NPN overlap syndrome and so it's although, again, this is not a common symptom and I don't have an answer for you in straight up MDS. It is seen in patients with MPN and there is this overlap. So, I don't know specifically in what diagnosis they've given you and whether you fall in one of these overlaps, but that might be what's going on.

Jean Ridgeway: You've certainly gone to some very reputable institutions to get diagnosed. (Attendee)?

Q37: Hi. I'm (Attendee), (Attendee)'s husband from Stafford, Connecticut as well. I'm here to gather some information to be able to help my wife in any way I can. If I weren't here I'd probably be in my basement workshop overhauling some summer furniture I've got underway, but as a former engineer I've listened to everybody around the room here and there seems to be one common thread that is more likely than everything else we've heard, but for the MDS and that word is 'golf.'

Jean Ridgeway: Very good. Very good. Okay. I'm going to just flip some sides over. It's about 10 minutes till 12:00. Would you all like to ingather your lunch and have a working lunch? You want to have lunch? You want to go till 12:00? What would you like to do?

?: (inaudible 1:43:19).

Jean Ridgeway: I have four children. I could do anything. It's not a problem. I once had four teenagers for two years. Nothing bothers me. Well, why don't we do that? Why don't we go ahead and start lunch? You guys go ahead and grab your lunches and once everybody's back around the table then we'll restart. Does that sound fair?

Everybody ready? Alright. We'll rock and roll. So, I've been asked a couple of things. (Inaudible 1:43:47) for those of you who would like to help everybody out and so it doesn't… there are no takeout bags, but please feel free to get some additional things to eat because there's lots more food than people have been eating. So, there's not as many desserts I did notice, but there's plenty of fruit and vegetables and some carbohydrates. So, please feel free to go back up and get something to eat and drink. So, it's 12:30. We'll interact for about an hour and there's somebody subsequent to me that's going to talk about iron chelation.

So, as everyone was mixing, I was talking to a couple of people in the back and they asked me a couple questions and I thought I'd just answer them in general. Maybe you have the same questions.

When initially this morning we all began to discuss things, names of drugs were thrown out there. So, folks were saying well, what are the other name? So, just like we buy Tylenol and we call it acetaminophen. There's a generic name and there's a trade name. So, there's a compound name. So, one of the questions was what are the names of some of these drugs? So, a couple folks have talked to us and told us that they're on Vidaza or 5-Azacytidine. Sometimes we call it 5-Aza. That's the other name for it and the other… a couple of the other drugs one of them was called Decitabine or Dacogen and the question that came was why are these drugs used pretty commonly? So, we talked about approved therapies for MDS. So, there's three. So, the other drug we talked about was they wanted to know the other name. Revlimid is Lenalidomide. So, Revlimid is the brand name. Lenalidomide is the compound name. Why are these drugs used frequently? They're approved by the FDA. So, they have a proven track record. You saw some of those graphs that they can treat and have success. So, those are the names of the drugs. Other names of drugs with the supportive care and we'll talk a little bit more about it one of it was Epogen or sometimes folks call that ESA, erythroid stimulating agent. Basically, they're hormones that encourage your bone marrow to make more red blood cells if you don't have a lot of that hormone. There's a couple forms of it. One is called Procrit. That's the trade name and then there's another longer acting formulation of that drug called Darbepoetin. So, that's the other name. GCSF, granulite stimulating hormone, GCSF is used. The other name for that is called Neupogen. It increases your white blood cells. There's a longer acting version of that that's used in oncology and it's called Neulasta. So, that's another… that's regulated. It's got a different formulation. CSA is cyclosporine. So, that's a drug that can be used sometimes. ATG. That stands for anti-thymocyte globulin. So, those were some of the names. They had some questions about that.

I think that one of the take home points besides (Attendee)'s astute observation that golf is definitely holds the room together the other thing about MDS is that we live with MDS and so I would echo (Attendee)'s insistence that people continue to live and do what you want to do and enjoy life because life is for living and enjoyment. So, I think that should be the banner of what we look at.

So, let me go over some of these. Now, that book in front of you has these different modules in it and it's really for you to help understand and the family givers… family caregivers. So, there's five different modules and little booklets inside of it.

The first one is really Understanding MDS. So, everything that was talked about this morning in the slides is in some way restated in this first module. So, if you were in college and all the kids take the notes and nowadays people don't go to school with pencil and paper. They go with their computer and all the slides are loaded on their laptop. So, you don't have to worry about getting the slides because everything that was on the slides is in the booklet. So, take a look at that. I also have to run up here and advance the slides. See if I can do this right.

So, this just kind of a reference point for you all. The effort to put this information together came from my colleagues with the International Nursing Leadership Board. So, MDS is a global disorder and people all over the world share your concerns and your challenges and so as a group we got together and over the course of a few years help to enhance what was already present, but then put something together because what we hear as nurses and nurse practitioners is that patients and patient's families want information.

So, we'll go over somewhat of the same information as you discussed this morning of people... So, some people in this room live with MDs. Many people in this room help care for people with MDS and one of the most common questions and some families that are recently affected with this disorder is why do people start treatment and so as it happens before they come and see hematology oncology there's a whole history behind that and I can't remember where I heard it, but someone in this room has a history that's very common what we hear in the clinic is that oftentimes MDS can be hard to diagnose that people don't perhaps don't feel well for a while, but no one's been able to put their finger on what the diagnosis is and that just getting the diagnosis of MDS often can be a journey in and of itself. Some folks are heading off to get a knee replacement or perhaps they see a new primary care provider and they draw a CBC and that kind of starts the journey. Other people may really not feel well at all and then they get a blood count checked or some people are unfortunate enough to be in the hospital with something else and unrelated and have a low blood count that gets recognized and then that's how they start, but after all that testing is done people are going to fall into really one of two big categories – low risk disease or high risk disease.

So, what's the difference and how do clinicians begin to look at patients through those two different perspectives? When people have lower risk disease what we know is we want to help the blood counts and we can do that through a couple ways using some of those growth factors, the Epogen perhaps the white blood cell count, perhaps giving people transfusion and people just have that anemia many, many times. About 80 percent of people who have MDS have low hemoglobin and low red count and so they get transfusions and some people like (Attendee) have had hundreds of transfusions. So, their transfusions are becoming… if you don't know, they're becoming a little bit more difficult to navigate from a patient perspective as our insurer payers are becoming more difficult with their willingness to reimburse for transfusions. The transfusions are readily accepted as therapy, an active therapy, but they can be a bit tricky. So, I'm not sure if… I know (Attendee)'s had transfusions. Other people in the room had transfusions? Yes? So, the first thing that has to happen is they draw a vile of blood, you get typed in screen. Where I work at an academic institution in a big city, we have a pretty good blood supply. This week for the very first time I've been there for almost 15 years we were told that the entire institution was out of platelets. We have no platelets at the University of Chicago. Blood supply is voluntary. There's always shortages in the summer, but it's a reality. There are other countries across the globe that when a patient is introduced to a blood disorder the family is highly encouraged to give blood. So, I would say that one of the things I talk to patients about is when families feel powerless and they want to help, I'm like, "Why don't you go ahead and

donate blood," or, "organize a blood drive." That's a big useful piece because your family member more than likely is going to be the beneficiary of a transfusion somewhere along the line. Very true. So, we look at people in our buckets of who gets treated and who doesn't get treated and when do they start. So, the low risk people we really want to get their blood counts better so we can give them Epogen which is that EPO shot and we can give them transfusions. Now, the thing about Epogen that the doctor alluded to earlier is that it's a hormone. We measure your level. So, I would say that measuring somebody's EPO level would be like pouring some ice tea into a container. So, if my container is all the way filled to the top it really doesn't benefit me to pour more in. Correct? So, if your EPO level drawn in your blood is of a normal level that should be stimulating your bone marrow to produce then if you pour more in it's really not going to help. So, that's why some people can get EPO or some people can't. When people start Epogen as an injection, we want to make sure that your red blood cells in your bone marrow have all the necessary building blocks to make red blood cells. So, that's folate, that's iron, that's B12. Those are all things that people can either have injections for or take by mouth to help build the red blood cells and then the Epogen gets given and you have to wait for about 12 weeks to see if it's really going to make a difference because that's how long it's going to take. So, it takes a long time. Now, during that time people can also get a red blood cell transfusion and the newest recommendation from the American Society of Hematology is that people should be able to adapt to a hemoglobin of seven grams per deciliter. So, anybody in this room ever had a hemoglobin of less than seven? How do you feel when your hemoglobin is down to seven? You feel pretty good. Anybody else? He was very tired.

Q38: Very weak.

Jean Ridgeway: (Attendee) was very weak and tired. Right. So one of the benefits is that you "may" feel better, but the true benefit why do we give you a red blood cell transfusion is to help your body work better because all of our organs need oxygen, our kidneys, our brain, everything, and so one of the muscles that's really important that needs oxygen is our heart. So, people who have perhaps a history of heart disease like if they've had heart attack are a little bit more sensitive, but that's what we can do to help the red blood cells and so a lot of people do get that.

Now, what about other reasons to start treatment? So, definitely cytopenia. So, when those counts go down, if the white blood cell goes down we call that neutropenia. If the red blood cell count goes down we call that anemia and if the platelet count goes down we call that thrombocytopenia. So, those are just words that help us identify what's going on and so when we look at progressive or symptomatic cytopenias it means that those blood counts are decreasing by quite a bit and they need some type of attention to correct them. Otherwise, without correction the consequences could have an impact on how people feel or how people's bodies are able to function.

So with low white blood cell count if you're low, in MDS we usually don't give people a lot of growth factor. It artificially raises the white blood cell count, but it's very temporary and so

when people's white blood cell count is low and you might be subject to an infection, honestly, the best thing you can do is wash your hands well. Family members what can they do to really help is make sure that everybody in your house hold or that comes in contact with folks are up to date with their immunizations. We should all get a flu shot patients included even if you have low counts. Dietary restrictions if your counts are low. Just make sure that your food is washed and if you're a sushi lover or clam… You cook clams. Right? You like steam them or you eat them raw? Both. Okay. So, you have to be realistic about food health. So, you don't want to leave food sitting around and things like that.

Other things with low platelet counts. Sometimes this gets a little more tricky for people who have MDS because if your platelets are really low, you may have to have some platelets before you go for a procedure. So, say you need cataract surgery, usually the surgeons… people will do brain surgery if your platelet count is 50,000. So, the eye doctors are good with having your platelets above 50,000, but that might need to be done. The danger with platelets is that you can be vulnerable to having bleeding. You just have to be careful. So, not everybody has all those counts are low, but some do. So, sometimes it's just those cytopenias that say we need to treat and more specifically if people are really symptomatic with their cytopenias. So, I've had some patients come and how they even get diagnosed with their MDS is that they've had a string of infections. So, maybe they had a pneumonia in the fall then they have a skin infection and then they get an eye infection and it's not until someone looks at their white blood cell count to identify that the cytopenias are caused by a bone marrow failure that they get the attention to try to correct what the true problem is instead of just getting another prescription.

And then you talked about this a little bit before you have to think about individualizing the treatment. So, your mom has high risk disease. Other people have lower risk disease or are stable without any treatments. So, when you look at how do you treat one person versus the next, they take in all types of factors into consideration. So, it gets very individualized and there's a choice of lifestyle. So, living in the Midwest like Boston our winters a winter and so we have people who go to Florida. So, they have a doctor in the Midwest and they have a doctor in Florida. We've got people who can you take time off of treatment? You can and then people get monitored with their CBCs as well. So, it's a lot about lifestyle and where do you want to go and what do you want to do and you can work with your provider and I would say I know we talked about like no doctor bashing, but if you or your family member is seeing someone and you don't feel comfortable, I think a couple of things that can help you feel perhaps that you have more influence or you have a better understanding of who the provider is, who the physician is is go to the appointment and ask some of the questions that are being discussed here today and if you don't… if you're looking for a second opinion, how do you go about getting a second opinion? I would suggest that you use the resource of the MDS Foundation and getting a listing of who in the area is considered an MDS expert. You call that office and say I'm calling to get a second opinion. They'll ask for records to be forwarded and then go for a second opinion and see what they have to say. Make sense? Questions?

Q39: (inaudible 2:02:01)

So, (Attendee)'s question is what are the fine political nuances of seeking a second opinion. Okay? I would say you just say I'm thinking I'm going to get a second opinion. Is there anybody you would recommend? Give them the platform. They may say yes or no, but I will say as a practicing clinician we always… we'll give a recommendation just say like are you looking at staying local? If your physician is shy about getting a second opinion, you should run to the second opinion. Don't walk, but run. So, no one should be threatened by it. It's a business. You get a second opinion on your car or all those other things. So, medicine is a business and it's driven by consumers and there's a fit and I'll tell you I work with 10 physicians and they're 10 very different people. I have men, I have women, introverts, extroverts, people who like to work with young adults, people who won't look at you until you're over 70. So, it's all about the fit and as a patient you really are… you don't want to say choice, but sometimes you really don't have a choice. You get assigned a doctor. You get seen in the hospital. You're discharged and you're told to follow up with Dr. X. So, don't be intimidated about getting a second opinion. In medicine it's very common. You won't hurt anyone's feelings. It's a little touchy though. I know this, but I just say I might want to go for a second opinion. I think that's great. I think that's great, but don't be like the girl who said to me this week who was supposed to start on her therapy. She calls me at 8:10 and I had her set up like she lives 70 miles away. I don't know what Boston traffic is like, but you can imagine what Chicago traffic is like. It's terrible and so she was supposed to start her treatment at 9:00 and she called me at 8:10 no joke and said, "I'm looking for a second opinion," and I said, "That's great. When were you thinking about going?" She said, "Today." I said, "That's great. Where are you going?" She goes, "I don't know. You have to tell me." Perhaps the discussion should have happened a little earlier, but anyway. So, that was kind of funny.

So, other choices about treatments, again, it's based on that IPSS score. Let's see if I can do this better. I'm really having technical difficulties and not doing so good. I'm pressing it really. Maybe there's a lock on. I was doing the number thing. Okay. Sorry about that. So, you talked a bit about this. So, allogeneic bone marrow transplant. Allogeneic is a big word that basically means you're going to get somebody else's stem cells not your own. There's a bone marrow disorder called multiple myeloma where people get their own stem cells and even in some lymphomas people get their own stem cells, but allogeneic means somebody else's. Many times it can be a brother or sister or it can be a sibling. That's a brother or sister. You can have children and then we can also do umbilical cords, but again there are a lot of factors that go into that not so simple. Is anybody here like in the process of transplant? They've been talking about transplant? We won't talk about it too much. It's kind of an entire… It's a whole subspecialty, so but it can be done.

Age shouldn't be exclusive for active therapies. Again, looking at people what their biological age is and how functional they are. So, I think that if I only know you when you're ill, I don't really know you and so what I'll say to patients is… So, here we are in June. So, I'll say, "Well,

tell me about Easter. What was like Easter like at your house? What was Christmas like at your house?" and that can give you a better tempo of how active somebody is because some people are super active. They're out golfing, they're working, but some maybe not. Maybe some people are really struggling with other illnesses alongside with their MDS that make it much more complicated and that's where those two words come fit versus frail and the other thing about MDS is some people in this room know well is that the treatments can take time to work. So, your mom just got at treatment with 5-Azacitidine. So, what we know about that and I'll show you some slides is that things usually get worse before they get better and why does that happen? So, in our bone marrow when you have MDS what's the driving force behind making all of your blood counts is something called the malignant clone. So, that means that the system cell… So, stem cells have this very unique ability. They either recreate or they start to grow up and due to various influences be it hormones, cytokines, nutrition, a cell becomes from a stem cell to a platelet or a stem cell to a red cell. When that stem cell has picked up a genetic error and you talked about the cytogenetics and genetic error, it's now considered malignant. So, it's not reproducing normally. So as you begin to get rid of that malignant stem cell, you start getting rid of all those other blood counts as well. Some people talk about that as an example of the garden and the soil and the seeds where the stem cells are the good seeds and the MDS ones are the weeds in the garden. So, we start cleaning out the weeds in the garden. So, I'm not a great gardener. I wish I was better. Somebody in here said they'd be in their garden, but if I go on vacation in July it's pretty warm. We get a lot of rain in the Midwest. When I come back there are a couple things happening in my garden. The weeds are growing way better than the plants. They should be growing like great. So, what do I do? I get in there and I start pulling out all the weeds. So then when I'm done and I look at my garden, the ones that are left look a little bit puny. They don't look so healthy. Why? Because the nutrients have been taken by the weeds and so many times in MDS what's happening is that those other cells are being… they're gaining nutrition from the bone marrow environment and what's left for the other ones is not so much. So, you start giving them therapy, you're doing weeding and then the ones that are left behind are a little bit weakened. So, we start to see falling in counts. So, people get treatment for a week usually if you're on one of those injections either the Azacitidine or the Dacogen and you get your blood count checked in a week and it's okay and then the second week the blood count is lower and then the third week they start to recover and how long does it really take to make a difference? What we know is that we need to give folks at least four to six months of treatment because each cycle is basically four weeks long before we know whether or not it's going to work. Now, a couple of things tell us if they work. Right? People feel better. Didn't you say that? Sometimes people's counts will get better at the end of the six months. We usually we'll ask the patient to undergo another bone marrow evaluation to really see what's going on inside the bone marrow. You're laughing?

Q40: (inaudible 2:09:54).

Jean Ridgeway: Oh. How far are you in your treatment?

Q40: (inaudible 2:10:00).

Jean Ridgeway: About six months. When do you see the doctor?

Q40: (inaudible 2:10:05).

Jean Ridgeway: Yeah. Don't be surprised… but you know what? I have to tell you and I will own it that I work at an academic center and so if you're in an academic center sometimes it's a little different than what's in the community and if you're on a clinical trial it really is driven many times by what the trial is asking. Sometimes in the community they don't ask for a bone marrow that your counts are going good then people will say you don't really need one, they're doing better. So, how long do you stay on treatment? You stay on treatment as long as the treatment continues to work for you without bad side effects. That's how long you stay on the treatment. So, you begin to look at MDS as a chronic illness and there can be interruptions. People can get an infection. Getting an infection in MDS is not so uncommon. People end up in the hospital. Then you need to recover from the infection and sometimes that takes weeks or months really depending on how severe the infection is and then the treatment starts up again.

So, the other thing… the last comment on that slide says that proactive management… better to report side effects early than late. So, what does that mean? So, when I meet with patients and they're going through treatment, I'll say to them if you develop a fever, if you're just feeling unwell, call us, we can see you, we can talk to you over the telephone and decide whether or not you need to be seen. So, little problems my philosophy in life is my dad was a mechanic and so little problems taken care of early have a far better outcome than problems that you ignore and take care of much later. So, that squeaky break, that flashing light…

Q41: I have a question. My doctor said that they can't do much about the white blood cell count. Now, I haven't heard anything. Maybe I'm missing something.

Jean Ridgeway: So, his comment is not much to do about the white blood cell count. That's true. So, you could… your doctor could maybe "make" himself or you feel better by giving you an injection of Neupogen, but it doesn't cure the problem.

Q41: Right. They did that once.

Jean Ridgeway: They did that once and at my institution we don't do that. There are other places that if you're not having a great response to like EPO alone they may add the Neupogen, but a white count that's really low in and of itself is not a predictor of getting an infection or how well you're going to do or not do.

Q41: Okay and then I have a second question and that is that my dentist said that I have a cavity that I should have taken care of, but the hematologist said no you can't, and so I guess the question is how long do we delay?

Jean Ridgeway: So, is it a cavity or a root canal?

Q41: No. It's a cavity.

Jean Ridgeway: Oh, cavities are fine. Do you have a port? Do you have an implanted port?

Q41: No.

Jean Ridgeway: Anybody in the room have an implanted port? So, if you have an implanted port you have to get antibiotics beforehand. If you're simply looking at a cavity you are fine to go to the dentist. I mean, the worst… I'm not a dentist. Is anybody in here a dentist? You don't want to get an infection and get an abscess.

Q41: That's why she didn't want me to… the hematologist didn't want me to go.

Jean Ridgeway: It's simply a cavity?

Q41: Yeah. Under my front tooth.

Jean Ridgeway: When are you going for the second opinion?

(Laughing)

I would say you're fine to go. I don't know what your platelets are. Are your platelets above 50? You're good?

Q41: I have it right here. (Inaudible 2:13:46) was 32.

Jean Ridgeway: Your platelets?

Q41: Yeah.

Jean Ridgeway: White count is 125. That's okay.

Q41: You think I could…

Jean Ridgeway: I think you could go… Your platelets are lower, but those are your platelets. You're obviously not bleeding. It's a cavity. I mean, you need to get it treated. Maybe the dentist

would want to give you some antibiotics like start two days before and continue for a couple days after just to kind of cocoon you for an infection. Anything else? No. Okay.

So, why is time required? So, this basically is a picture of what we talked about. So, before the treatment begins and the blood counts are where you start. So, everybody has the starting point, but no one is going to start at the same place. So, what this shows us really these nice great big red disks those are your red blood cells and these bigger ugly cells those are the MDS cells. These probably are platelets in here and then in the background. So, what happens is that the MDS cells are really crowding out the normal cells in the bone marrow. So, this is kind of a funny looking cell. That's probably another one. So, you have a busy full bone marrow. Then what happens is we start treatment. So, when you start treatment you're going to see the second panel has a lot of these other cells removed both the red cells and then the platelets and these other ones and up above is a picture of an actual patient and what happens during their treatment. So, ANC stands for absolute neutrophil count. When you get a CBC done there are a lot of different descriptions of cells on that. The four ones that are most important, one is the total white blood cells, the other one is the hemoglobin and the platelets and then the absolute neutrophil count, neutrophils are the white blood cell soldiers fighting infection. So, about 85 percent of all of our white blood cells are neutrophils. Sometimes they're called granulocytes. So, it may say absolute neutrophils. It may say granulocytes. One or the other and we look at that because it can help us understand infection. So, this is a picture of what happened with this person's blood count. So, at the very top they're starting… their total white blood cell count or their absolute neutrophil count is 3,000, 3.2 and then over the course of treatment and weeks. So, the bottom one is telling us that here's six weeks. So, what happens during all of that treatment is it goes down, down, down and then it begins to rise up. So as the person goes forward from there then they have more healthy cells that can reproduce. So, it's not uncommon at all for people to have really low blood counts for a number of weeks or months and it doesn't mean the treatment isn't working. It's just the biology of how the drugs work. So as it begins to regenerate, blood counts should improve, things should get better and then at the completion of four to six cycles is what you have is the elimination and the last panel really doesn't have these MDS cells anymore, but it has more healthy red cells. It has more healthy neutrophils and then platelets as well, but it's going to take time and many times people get discouraged because it's not encouraging to see your blood counts go down. We live in a culture that we press a button, we can find our directions. We live in an instant society and this is not an instant treatment. You need to have a lot of patients and so does your caregiver and your family to have an understanding that things take time.

Where do people have problems? They have problem's here. Right? So, when you start treatment and you're counts go really low that's when you're more prone to get an infection.

So, it's that time in the center and getting through this low point that you'll need to work with your healthcare team for the best response. So, sometimes the counts can go…

Q42: You said it takes up to maybe six months?

Jean Ridgeway: (Agreement sound)

Q42: Now, he was diagnosed in September and he goes every single Monday since then and gets a Procrit shot and his numbers start every single week it goes down, down, down just a little till he has to get a blood transfusion. Is that considered working?

Jean Ridgeway: This isn't Procrit. This is looking at getting treatment with like Azacitidine or Vidaza. So with the… If somebody's getting Procrit and he started in September. So, it's all of September, October, November. So, that's three months. Has he needed less red blood cells?

Q42: He's had three transfusions since then. Three. So, it just goes every time he goes if it goes down a little…

Jean Ridgeway: The hemoglobin is going down and down?

Q42: Yeah and then until it gets too low it's dangerous and he has to get the blood transfusion then they start him… It's been just the same cycle since September.

Jean Ridgeway: Okay.

Q42: I just wanted to know if that was considered working or…?

Jean Ridgeway: Right. So, (Attendee) do you want to say something?

Q43: I'd like to offer from my experience that I've had periods where I could go for 12 – 13 years with no transfusions and I've had times when I've had to have five a week and the cycle and now I'm back in a cycle I've only had two this year and one was because of the surgery from a smashed elbow and it can vary a great deal and they're long cycles where you can go up and down and I had one case where I was taking Celebrex after I gotten transfusion independent and 11 tablets and I ended up in the hospital and had to have eight units to get myself up to a safe level of eight because the Celebrex has COX-2 inhibitors which affected me personally. It's like an allergic reaction, but I wouldn't be concerned at the kind of levels that you're talking about personally. Of course, you have to deal with your doctor and find out, but I've had a wide, wide range of transfusion needs.

Q42: It's just that it affects your life when you have to go in every single Monday to get the shot that doesn't seem to be really working. It just goes down, down, down, down till it's time for a blood transfusion. Same thing. Every like six… is it six weeks maybe?

Jean Ridgeway: The goal of the shot, the Procrit shot, is to help decrease the need for red transfusion. If the only thing that is wrong is that he's low on the hormone then by giving the hormone it will correct. What happens though is it's not the only problem. So, it sounds like your doctor is using the Procrit shots to help support him and then he still needs red blood cell transfusion. So, I think a couple things perhaps to ask the doctor would be there's a kind that you can get that's longer acting. Could you switch to the longer acting type of EPO, so you don't have to go every week and then do you feel like short of breath and are you tired when the blood cells go down…?

Q43: (inaudible 2:22:42) very well.

Jean Ridgeway: Tell me what your level is that he transfused you at. Eight, seven?

Q43: Yeah. They're sevens.

Jean Ridgeway: Sevens. It's seven. So and honestly at our place if you're in the sevens, we leave it up to the patient because there's… there are risks associated with red cell transfusion and over the long term it's iron (inaudible 2:23:09) because every time you get a unit of blood you get a lot of iron and iron isn't naturally excreted from our bodies. So, it will deposit itself in other organs like the liver or the kidneys, the testes and then at a certain point there's a measurement that we can do called a ferritin level that if the ferritin level begins to get to a certain number it's suggested that you help rid the body of excess iron through something called chelation and you can do that intravenously or orally. So, but you've only had three transfusions?

Q43: I believe it's only been three. Yeah. It's every three months maybe.

Jean Ridgeway: The good part about only having to come once a week is only having to come once a week.

Q43: Good point.

Jean Ridgeway: You come in. You come in for a CBC. I don't know what the turnaround time in your clinic is. Our clinic maybe 20 minutes. Other places is if they have the machine right there it's like 10 minutes, but now when do you meet with your doctor again?

Q43: Monday.

Q41: Every Monday.

Jean Ridgeway: Oh, you meet with him every Monday?

Q41: Every single week he goes for the Procrit shot.

Jean Ridgeway: Well…

Q41: I just wanted to know if that was normal for MDS patients because it does affect his lifestyle because it's every single Monday he has to go and he does let his blood get dangerously… It gets to the point that the doctor is yelling at him that he has to have a blood transfusion because he tolerates… He doesn't get tired or… he tolerates it very well.

Jean Ridgeway: People can that accommodating. So if you and I had a blood… if our hemoglobin dropped to seven tomorrow, we'd be horizontal, but you accommodate to these… it's kind of like the frog who gets boiled in the pot. You just like slowly accommodate. So, your body gets used to it, but seven, 6 ½, seven is where people begin to strongly suggest to get a transfusion. I leave it up to my patients. I saw a guy yesterday. I worked all day yesterday and then I got on an airplane and came here and somebody I saw he was seven and I said, "Well, do you want to get transfused today?" We have the ability to transfuse people over the weekend, which I think sounds like a great idea and he said, "You're going to ruin my weekend. No. I'll do it today." Okay. Fine. So, it's a bit of a negotiation. Here's what our options are. What do you want to do?

Q43: I do have to say that they always give me the option to either go or not go and I say no, I feel fine.

Q41: Until they tell you have to go.

Q43: Well, that's when they pick me off the ground.

Jean Ridgeway: Yeah. That's not good and that's what your wife wants to avoid because you make her nervous. The caregivers in this room are kind of… they sit on the edge of their seat because they don't quite know what to expect, but it's pretty nerve-wracking to be a caregiver.

Q43: (inaudible 2:26:25).

Q41: Do you go every single week to see your doctor?

Q43: No. I have the other, Vidaza. I go for one week and I get shots in my stomach for five days and then I'm free for three weeks.

Jean Ridgeway: To give the EPO. So, Epogen is a red blood cell… It's a hormone that stimulates your red blood cells and so why you have to have your blood tested is if your hemoglobin gets to 12 grams or above then they're not going to give you any, but how do they know what your hemoglobin is when you come in for an injection rules they test it? So, that's why they draw the CBC. So, it's the catch 22.

Q44: One thing I would suggest is keep track of your counts, your ANC and your platelets and your red cells and see how you do and see how you feel. You can kind of keep a log. I was really bad… Well, I still am about keeping my records and my stack is about this deep of paperwork and I started charting it and you can see patterns of how you feel and judge from that and it can change over time, but there is a lot of variation over periods of time. I'm almost 24 years now and it will change. You'll see up cycles, down cycles and ripples, but you just have to… If you're comfortable, I'd say go with the way you feel and your doctor.

Jean Ridgeway: Good advice. Good advice. And in one of the packets in the booklet is actually I think towards the back is how to like track your counts. So, your medical records belong to you. So, it is perfectly permissible to say can I have a copy of my counts from today and you can tuck them in a folder, you can plug them into a phone. Some people do Excel spreadsheets, but I agree. Having your records… even when you have your bone biopsies and you should get a copy of the report and keep it then when your family wants to know what's going on you can pull it out and show it to them. Now, you might not be able to interpret it and that's okay, but that is information that belongs to you and there is a spectrum of what people want to know from just do what the doctor says to scrutinizing every test in question. So, everybody falls somewhere in that spectrum. Does that make sense? You're like the picture…

Let's see what else. So, we talked about tracking. So, here is somebody who was an engineer and tracked their counts. So, let's get a picture of over time what happened to this person. So, this actually… So it's a graph and on the bottom it's time across the bottom and then there's both the… So, the hemoglobin is the purple boxes, the platelet count are the yellow triangles and the white blood cells are the black diamonds and so this person gets referred, they get a diagnosis and they're being watched. So, this is back in 2010 and it goes then all the way through 2011. So, over a year. So, this person has to initiate therapy. So, that does not sound like your case. You're getting supported. So, I'm going to put you in the bucket of the low risk person. You're getting treatment with EPO and transfusions but you're not getting treatment with Azacitidine like other people are. This person though gets started on treatment. So, here are their counts beforehand. So, where are they? Are they normal or are they not normal? So, you can see down here this is the white blood cell count. This person, the average… not the average. The lower end of normal white blood cell count is actually 3 ½ all the way up to 11. The triangles are the platelet counts. So, platelets reference is over there. So, you can tell the person is consistently under 100,000 and then the hemoglobin, they start at 12, but then they drift downward. So what happens over time to this person is you see variability. So, you talked about variability in their blood count. That's exactly what we see here. We see the blood cell count go up and down and up and down and I would bet that during these super low points the person got transfused. Here with the platelets same issue. We see they started higher when they were first evaded and then they kind of dropped and they went up and down and not until cycle three and four do you really see a more normal platelet count. This person's HCT means they got a stem cell transplant. So, they got somebody's new stem cells and whole new way to create blood cells. So, then you see

super normal because they've now had somebody else's, but during this time of therapy you see persistently low counts until about cycle three and four and then you see more normalizing of counts. So, to know that that's… this is somebody who's on therapy with Azacitidine. So, we're fixing the factory, we're cleaning out the garden and then things got worse before they got better.

Now, we talked a little bit about this, but not so much. Lenalidomide or is the drug called Revlimid. It's a pill. This pill is an analog or a sister medicine to a drug called Thalidomide. So, Thalidomide babies were the babies in the '60s that were born with truncated limbs. Remember that? And that's because what happened was through that misfortune they found out that the drug itself can cause a decrease of blood supply to be offered and so these newer drugs are used therapeutically for the benefit of those side effects. So, this and it's specifically approved for patients with that cytogenetic five… they have a chromosome 5Q abnormality. So, you take pills for that. So, this person has been on therapy for almost 10 years with Lenalidomide. So, an oral tablet and the same kind of thing. You can see that back at the beginning they had a relatively normal platelet count. It dropped. Now, these are years instead of weeks or months, but you can see that it's been over the course of years until that person had an improvement in their platelet count. The same thing with their hemoglobin. A drop and then their new normal is 11 grams per deciliter, which if you read a text book you'd say the person was chronically anemic but not in need of transfusion and this last box down here the white blood cell count you can see barely ventures into the normal range all throughout the trajectory of therapy, but so that's how tracking counts can really help and how long do people stay on therapies? People stay on therapy for a long time.

What can you do to stay healthy? I would definitely say stay active. Keep going with what you enjoy doing, a (inaudible 2:33:57) golfing, clamming. I don't know anything about clamming. Eat a balanced diet. Is there a diet? No, there's no diet for you or me either. So, what you want to do is just be sensible. Have balanced vegetables. You want to eat a more holistic diet. So, keep a good weight. Avoid junk food. Not too much alcohol. What about activity and exercise? Yeah. Be as active as you can be, as you want to be. Certain things should they be limited? If you have a low platelet count, should probably avoid wrestling, rugby, but playing golf or swimming, etc., keeping healthy and getting rest but not too much and staying in contact with your healthcare providers and that letting them know what's going on when it's going on. So, if you think you're having a problem, just pick up… hopefully, you have a good enough relationship with your interdisciplinary team that you can pick up the phone and just make a phone call and say I have this terrible sore throat or like, you know, an earache. In our center if we're taking care of you and you call me and you say these are my symptoms, I see you. I don't ask you to turn around see your primary care physician because you're different than just your ordinary primary care patient. So, I'm not quite sure where you fall into that, but again little problems taken care of earlier can have a better outcome than ignoring something.

Q45: One of the things that seems to be coming through and (Attendee), you seem to be making this point is that are we basically adapting to lower levels of various measures like, for example,

my white blood count is lower and my provider gives me what the standard range is. Now, I probably will never get to the standard range, I gather.

Jean Ridgeway: Maybe. That's true.

Q45: And so you just sort of live with it. You don't just expect to get back into the normal range.

Jean Ridgeway: Correct. I would say that in some instances that's very true. Your normal may be that you're more anemic than a man of your age without MDS, but it shouldn't be limiting. Your white blood cell count is low, but don't lock your door and live in your house. That's I want to say. Like don't let it be so controlling that it's going to totally limit what you're able to do or not to do. Does that make sense?

Q46: May I offer one thing. A simplest example and I've had this because I go out to the Rockies is when you go from here at sea level to Denver and higher you go up to… In Colorado, I've gone up to 9 ½ to 14,000 feet and you can tell the difference because the oxygen level. That's the best analogy. If you go from here and go to Pikes Peak, you're going to have a tough time.

Jean Ridgeway: So, altitude and anemia. So anybody all of us who live in the flatlands when we go to a higher elevation we have a harder time acclimating to the available oxygen. So, since red blood cells carry oxygen if you have less of those to begin with acclimating to a higher altitude will be more difficult definitely. Definitely. But doing what you want to do is what your life should really be about. So, how do families stay engaged with that and so how can families be supportive? I would say that families should support people wanting to remain active. If you want to go to the golf course, go to the golf course. If you want to go do something be involved with family events those are all realistic scenarios that we all live with. Going to graduations and weddings. If somebody is arm's length away from you. So if you have a lower white blood count, are you at a higher risk for infection? Yes, that's true, but if people are at arm's lengths away and they're not actively coughing on you you're relatively protected. So, know that's very much true. If you have big families with sick little kids having sick little kids around people who have a lower white count is not ideal, but how do you manage that in a family situation? You can certainly tell children of certain ages, but then good handwashing and a little bit of separation if someone is like actively ill. Certainly if you have a child that has measles, don't bring them around somebody like (Attendee) who has a low white count. That's not a good idea. Patients should still go to family events and be involved in things like that.

So, there's also within the second book in this *Building Blocks*, talks about seeking treatment. The third one is about quick tips and quick tips in here really talk about some of the common issues that people have and I think the most common symptom that people with MDS struggle with is tiredness or fatigue. So, how do you manage fatigue? Anybody what to chime in what are some tricks that you've learned along the way? How do you take care of yourself if you're tired?

Rest. Correct. Is there too much rest? Yeah there's too much rest. Do not like wear the pajamas all day. I would say you should definitely get up every day and get ready for the day. So, part of feeling better is being active and engaged. So, do get up and get dressed and be involved in things. Taking a rest when you need it most certainly. I think if people go for walks, I think that's great. So, remaining active is another part of it. Don't rest too much. Exercise. You guys have Silver Sneakers around here? Do you know what that is? A lot of YMCAs and healthcare places are having classes for patients who are like over 60 who have cancer related diagnosis. So, they're more gentle exercises. So, getting involved in something like that.

Other tips for when you're tired. Nope. Just stay engaged. Stay engaged and if you're really feeling tired and you're feeling short of breath then if you haven't had your blood count checked in a while you may want to call your provider and say oh, I wonder if I need to come in for a CBC. I'm just feeling kind of pooped and see if you potentially might need a transfusion.

So, there are things in here about quick tips and then book four talks about iron overload. Somebody else is going to talk to you about that and then the last book is really in here is one of the ways that you can use to track your own healthcare. At the beginning there's some places just to put in for tracking your treatment, when did you start it, what treatments are you getting, what about your blood counts, etc.? If you're techy and savvy, you can go on the Internet or download an app. So, there's some other things out there as well for you.

So, these are just some of the things we've talked about before. If you're interested try to understand the disease and I think part of the reason we see families really involved in patients as well is that you want to know what's normal and what's abnormal. Correct? You want to know if this is totally normal getting EPO and still needing transfusions, being tired with treatment. It's normal. So, getting to know what to anticipate and know when to call the provider. You want to know about if you're in a treatment you want to know about what's the schedule. So if somebody's just started treatment is it five days? Is it seven days? Is it given every 28 days? How often is it given? And then all these drugs have some side effects and how do you deal with some of the side effects.

Q47: I was just wondering some of us sometimes will have a cup of coffee or drink caffeine. Is that verboten?

Jean Ridgeway: No.

Q47: Pardon?

Jean Ridgeway: That's fine.

Q47: It's fine. It's fine to have coffee, but I'm just wondering are there any other dietary restrictions in one's normal diet that we should be conscious of…?

Jean Ridgeway: So, it depends on if your white blood cell count is low the only thing you need to be careful of if your white count is low is that you shouldn't eat raw fish or chicken. So, those people who are sushi lovers just make sure that it's reputable. Fresh fruits and vegetables are fine. Just make sure that you wash them and you don't want to ingest something that could be harmful because if I acquire a foodborne illness, I can usually recover within 48 hours. It may take you two to four weeks. So, that's the only piece of it, but if you're cooking at home and you're cooking whatever there's no data to support it, but there are people all along that spectrum. There are people who are like you can never eat anything that's grown in the ground and that just is not standardized and most of the large academic centers which tend to be the thought leaders have really gone away from that. One of the things I would say is just make sure that if something sounds too good to be true like an herbal supplement or some type of something that's very different be very cautious because some of those things can be potentially harmful to you and might increase your risk of bleeding like St. John's Wart is something people for a while was a big rage about… you have to be careful about some of those things. So, either read carefully. The NIH actually has an app about these "alternative" type of therapies and potential interactions. Let people know what you're taking and what you're not taking both your primary care doctor and you oncologist. We usually pretty much that's the list anyway.

And so this is just the MDS plan. That's the fifth little booklet and Understanding Your Diagnosis. Make copies as well.

If you haven't gone on the website and you would like to there's a virtual support network on there so you can talk with other patients and then Audrey and Sue can help you contact and get you connected with the advocacy program as well.

So, I believe you have evaluations that got handed out. Is that right, Sue? So, they'll collect them or there's an electronic evaluation. I don't know how many people took a look at that, but that's available as well and so in closing there's someone else coming behind me, so I want to be sensitive to their time. Other questions? Comments? Things that you'd like to discuss that we haven't had the opportunity to? No?

Q48: What does the CBC or CBC that you mentioned?

Jean Ridgeway: CBC. So, that stands for Complete Blood Counts and it measures hematology values, very common hematology values. So, it tells what the white blood cell count is, it tells what the hemoglobin is and it tells what the platelets are and so that's a very routine, it's a single three CC blood vial, but then that determines do people need a transfusion? Are their white counts low? Platelets low?

Q49: Can I reiterate a little bit of what you said to the new people? From day one, we both read the book twice. We both did.

Jean Ridgeway: Which book.

Q49: The one you just gave us. *The Building Blocks*. I hope you have that. We both read it twice, my husband and I and we got to understand little more and from the time he started his shots and his blood work it says in there somewhere to take a three ringer binder, ask the nurse, the hematologist or whoever takes his blood to give you a copy of the printout and they're fatal to that and they give it to me and I have from day one to the last one he had. He's going back in two weeks for his blood. I have them all. I can compare them. I've even brought that book the emergency room with me and they were so thankful because the computers aren't friendly together from one hospital to another and I'll tell you you have everything in that book even when he had his bone marrow extraction. He had two. I got those results also and they're all in there by date and it's so helpful. It really is.

Jean Ridgeway: The other thing that might be helpful that's out on the table for you to take is this book. It's called *100 Questions & Answers About MDS*. So, it's the second edition and it's written a question and answer format and it asks all the questions that you want to know. How often will I need a platelet transfusion? What about chromosomes? What's ATG? What's a clinical trial? So, grab one of those if not for yourself, someone else in your family. It's an easy way to get reputable information. I guess that's the other thing I would say. I'm not a very computer savvy person, but I know enough to know that there's information out there that really isn't very helpful. So, looking at websites like the MDS Foundation and they have interactive education at many levels from patients to providers on there as well as the Leukemia Lymphoma Society and there's another large group called the AAMDS, Aplastic Anemia and MDS Foundation. That also has reputable information as well. So, as a support person or even as a patient just make sure you stick to the good stuff and not get distracted.

Q50: Can you just outline if there are any risks involved in participating in a clinical study?

Jean Ridgeway: Oh, wow. Now, that's a totally loaded question. Are there risks in a clinical trial?

Q50: Or could you just summarize it quickly?

Jean Ridgeway: So, it depends on what type of clinical trial. Know that the FDA is not going to allow something to happen that's going to be potentially harmful to you in a very negative fashion. There are so many built in checks and balances in these clinical trials and they evaluate everything so very carefully that I would say don't be fearful that it's going to harm you. Many times it's the only way to potentially get an agent. So, it may be evaluating the gold standard versus the new drug and so the only way to potentially get the new drug is it going to be positive or negative? Every drug has their own potential side effects. It may cause nausea and vomiting, but so do some of our available agents as well. If at any time during a clinical trial they do these

they're called interim analyses. They look at the data. If something is shown to be harmful then the study is stopped and the word gets out in the matter of minutes or hours to all the sites that everything has to be stopped. On the other hand if something's shown to be very beneficial, the FDA will say this is so good we're going to approve the drug and it'll go fast track. So, they're going to expedited approval because it takes many, many years. So, I mean, there's many risks. Lots of confidentiality. People sign something called an Informed Consent and it is very, very tightly scrutinized by an investigational review board at the institution that reports to the federal government. So, they're very tightly controlled. There are risk and every agent potentially holds its own risk. It's a risk benefit. Do you want to try this or don't you. So, that's kind of a longer answer.

Well, I'm going to step out so the next person can step in, but thank you again for coming and good luck in your journeys.

(Applause)