



Speakers:

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Tracey Iraca: Good morning. Hi, everyone. I'm Tracey Iraca. I'm the Director of the MDS Foundation. Just wanted to thank you all so much for coming this morning especially in this weather. I'm from New Jersey, so I get to have this weather today and then again tomorrow. So, I will appreciate it twice, but thank you so much for coming. I'm here with Deborah Murray, my colleague that you met outside. If there's anything that you need through the course of the day you can find myself or Deborah and we're happy to help.

Going to keep a casual atmosphere today. If you have a question raise your hand. Deborah and I will find you and we'll have microphones because we're audiotaping today's event. So, it's... so that we can post it on our website for folks that aren't able to come to the meeting, but they can still have a transcript and see what happened in the course of the day. We also have a poster you may have seen in the back. Wednesday was officially MDS World Awareness Day. So, if you're willing at lunch time perhaps we can take a nice big picture with our poster and we can post it on our social media sites and share it with other patients. We're doing everything we can to spread awareness of MDS worldwide and year round. So, wear your buttons proudly. We also have evaluations of today's events. We'll be handing them out for you to complete after lunch, but at lunch time we'll give them to you and then Dee will collect them at the end of the event. It's just kind of any suggestions you have for future meetings, any additional questions you may have and just a little bit about ways that we can improve our programs. Our special thank you to all of our sponsors that we offer these events free of charge because we have sponsorship and because of donations from very generous people. So, thank you to all of them. I want to thank our speakers and everyone who here today. We have Dr. Arellano and Dr. Langston who will speak first and then Nurse Sara Tinsley will speak after. We're going to be a little flexible with the agenda today depending on your questions, but again please feel comfortable to ask. That's why we're all here. If there's anything more. The restrooms, I think you've probably already found, but outside and to the right. Nice and easy. If you're hungry get up and get something. Just enjoy your day. If you need anything come find us. Thank you.

Amelia Langston, MD: Thank you. Thanks, everyone for being here. My name is Amelia Langston and I'm one of the hematologists and transplanters here at Emory. This is my colleague Dr. Martha Arellano and we're going to kind of tag team this today and try to talk about MDS. We only have one rule and that is that there's no rules. This is really for you and so I want people to feel free to interject, ask questions. There's not going to be a test at the end and... but really we're just trying to give you some information to service as sort of a springboard for your questions and I know that there will be questions both during the presentation at the end.

So, the topics we're going to talk about today really are we'll start with a little bit about MDS itself and what is it, talk about the diagnosis and how we make that. We'll talk about the different subtypes, prognostication and then we'll finish up a discussion of some of the treatment ops. So, we'll talk about treatment options both medical and stem cell translation, a little bit about clinical trials and then we'll finish up with a discussion of quality of life.

So, the bone marrow which is really what we're dealing with here is the blood factory. Its job is to make the different types of blood cells specifically the white blood cells that fight infection, the red blood cells that carry oxygen and the platelets that help the blood to clot.

Now, I think one of the important take home messages here is that MDS is not one disorder but really a group of disorders that have some common themes. The first theme is that in general the bone marrow is functioning poorly in doing its job of making the blood cells. So, there's generally a deficiency in one or more of the lines of cells. The cells often look abnormal and there can be a type of cell called the blast circulating in the bloodstream and we'll talk more about blasts in a minute. The other problem that people get into with MDS is the propensity in some patients to evolve from just a marrow insufficiency problem into frank acute leukemia.

Now, the bone marrow exists inside of the hollow part of the bones and basically, again, what's going on in there is that the bone marrow is making the red blood cells, the white... the various types of white blood cells and the platelets. Now, within the bone marrow normally there are these cells that we call blasts and everybody's got them, but under ordinary circumstances we have a very, very small number and those are kind of the seed cells, the raw materials that are maturing into these other kinds of blood cells, but what happens in MDS and in acute leukemia is that those blasts accumulate because the cells become arrested at that very primitive stage and when those blasts become to predominate that really gets in the way of everything else doing its job and if the blasts reach a point of 20 percent or more then we define that as being acute leukemia.

Now, MDS is a malignant disorder, but what does that really mean? What that means is that it's really derived by a series of genetic events that is changes in the DNA of a normal cell that as a consequence lead to the accumulation of abnormal cells in the bone marrow that no longer can do the normal job, but it's important to remember that just because this is a cancer doesn't necessarily have anything to do with how a person is going to live with the disease or how long they're going to live or what their quality of life is going to be like.

So, in MDS there is damage to the stem cells of the bone marrow. There can be these immature blasts that can come to predominate and the types of problems that people get into anemia which is low red blood cells, neutropenia which is low white blood cells to fight infection, thrombocytopenia refers to a low number of platelets that help the blood to clot. If all three of those lineages are down we call that pancytopenia and, again, when those blasts come to

predominate in the blood or the marrow then we define that as no longer being MDS but being acute leukemia.

Martha Arellano, MD: So, we decide to tag team this today because that is how we do it in the clinic. So, the hematologist works hand in hand with the transplant doctor to manage these patients. So, that's why we thought this was appropriate and thank you so much for having this event for our patients.

And so how common is MDS? How big of a problem? There are about 10,000 new cases per year in the US and about 300,000 to 400,000 cases in the world to date. They're about 10 to 20 percent of those cases are what we call secondary MDS which was caused by a specific thing that that's generally chemotherapy or exposure to radiation and that's one of the problems that we're seeing an increase as the treatments for other cancers get better then more patients are exposed to... as more patients are exposed to those treatments, we're going to see an increase in MDS cases. So, to give you an example breast cancer is about one in eight women. So, one in eight women will get breast cancer in their lifetime. They'll get chemo and radiation and most of them and then they have... it's a small chance, but it's a real chance of getting MDS or acute leukemia. It's less than five percent, but for that person that gets it it was 100 percent and so when I see a patient that has that history they'll say well, I shouldn't have taken that treatment, but that's not really a case because if they hadn't take then their treatment for the breast cancer six years ago they wouldn't be here today. So, it's a small risk, but it's a real risk that I tell patients to ask about so they can make informed decisions. In about 75 percent of patients are over the age of 60 and so when people ask me why did I get this? What was my risk factor? It's really getting older. So, most patients with MDS are in their late 60s to early 70s and that's the main risk factor. There are several effective treatments and this is one of the diseases that was sort of neglected for a long time and we're thankful for people like the MDS Foundation that have made this a priority and we're seeing now some developments coming out. So, people are getting excited about treating MDS and Amy will talk about transplantation which to date is the only potentially curative treatment for MDS, a donor transplant.

And so what are the causes and risk factors for MDS. So, there are three general types, really two general types. The other one is exceedingly rare. So, there's primary MDS that some people call de novo meaning there isn't anything that can be pinpointed as having caused it. So, we can't blame it on anything specific and that's the most common type of MDS. So, no specific known cause. One risk factor and this was recently in the news that repeated exposure to benzene which is found in cigarette smoke may be a risk factor, but it's very hard to pinpoint it because a lot of people smoke and most of those people will not get MDS. Lung cancer is more of a direct link to cigarette smoke. Then the other type of MDS is secondary MDS or the treatment related type of MDS is much less common than the primary or de novo MDS and chemotherapy and radiation therapy are risk factors. Inherited MDS is exceedingly rare, extremely rare. We may see one...

Yes, sir? You have a question.

Q1: If you had MDS in a family, two brothers had MDS what is the likelihood if you know of the children either the male children or all of the children coming down with MDS if it's already in the family?

Martha Arellano, MD: So, we've only seen I have seen two families that have what we call familial or inherited MDS and in those families everybody so Amy actually you took care of a family that had the son, the mother and I think the sister had MDS and so to be honest with you I don't know specifically what that number would be, but I would suggest some genetic counseling for that family.

Q2: Is there an identified factor (inaudible 12:39)?

Martha Arellano, MD: There are... So, this is not something that we would screen for, but I think in a case where you think that this might familial there are some specific mutations that are associated and seeing a genetic counselor they can come up... there's a panel of genetic mutations that they can check for and they can advise what treatment if any, is needed at that time.

Amelia Langston, MD: And I might add for the majority of cases of familial MDS we're talking about people getting MDS at a time when it's very (inaudible 13:26) I think they can hear me... when it's very unusual. So, in general familial families in which MDS runs they're not getting MDS in their 60s and 70s and 80s. They're getting MDS in their teens and 20s and in that circumstance when a child or a very young adult presents with MDS whether they have a family history or not there's a much higher probability that they have an inherited susceptibility, but for, let's say, two brothers who both got MDS in their 70s that's probably bad luck.

Martha Arellano, MD: Yeah. Probably random.

Q1: In a large family only those two had it probably then the odds of either one of their families getting is pretty small.

Martha Arellano, MD: Very rare like Amy said it's probably random.

Q1: Thank you.

Martha Arellano, MD: And so like I already alluded to the risk of MDS increases with increasing age. So, if you look at... so, this is the incidence. So, the number of MDS cases out of 100,000 people. So, for someone that's under 40 years of age there's almost a zero chance of getting MDS and if they do then you worry about that familial and then the risk increases. So, this is about one case per 100,000 and then as we get above 60 then our chances increase to the point where we're above 80. It's 55 people for every 100,000. So, it's still rare, right, 55 per

100,000, but the risk does increase with increasing age and that's one of the challenges with treating MDS that MDS in a 30 year old that doesn't have any other issues we kind of know right away what treatment. You want to hit the most... with Amy's treatment. Right? But a 90 year old that gets MDS and may have lots of other problems, diabetes, high blood pressure or things like that is trickier to come up with an effective treatment.

So, what are the signs and symptoms of MDS? Signs are things that you see or that the doctor will see. You look pale, you have a lot of bruises, things like that and symptoms are symptoms that we feel like shortness of breath and things like that. So, some people have no symptoms and probably no signs or symptoms at all at the time they get diagnosed. You might be just trucking along doing your daily thing and you go for a routine physical and the doctor says well, you know, you're a little bit anemic but not enough to have symptoms. You're red cells look a little weird and your white cell might be a little bit low, nothing that we need to do anything about. Let's just keep an eye on it. So, that's normal and then things kind of get worse from there and other patients have a lots of symptoms like this little guy. So, they may have fatigue. So, and these are the symptoms related to what's going on with the blood counts. So, if your hemoglobin is low you're going to look pale, you may have shortness of breath, fatigue, dizziness. If your neutrophils are low you may get an infection easily and this is how a lot of patients come to be diagnosed because they had an infection and if the platelets are low you might have excessive bleeding or unusual bruises. Bruises are normal, so don't panic if you have a couple of bruises, but if you have lots of bruises and they're in unusual places that might be due to the platelets being low.

And so how is MDS diagnosed? So, the doctor is going to do a physical exam looking for signs of something else like enlarged lymph nodes, unusual things. They're going to do some blood tests usually or you have to have a complete blood count looking at all the blood cells to make sure they're normal. There may be additional testing to rule out other causes of the low blood counts like vitamin deficiencies or infections, things like that and then if all that is normal and we don't find a cause then we're going to want to request a bone marrow test, a bone marrow biopsy and this is called bone marrow aspiration and biopsy and so the biopsy is a little tiny core of the bone marrow usually from the hip bone because that's the easiest place to get bone marrow from and the aspiration is they suck out some of the cells. So, those cells look... go to the pathology lab where usually Amy and I like to look at those because we just like to although we don't have to and we want to see what the cells look like. So, are they dysplastic? Dysplasia means they look bizarre. So, do the cells look bizarre or do they look normal? The chromosome analysis comes out one to two weeks later and we want to see if they're normal or abnormal and I'll talk a little bit about chromosomes in a second. Genetic testing is also helpful because sometimes there are specific mutations that the bone marrow cells, the MDS cells have and this test can also be done in blood when it's too difficult or it's contraindicated to get a bone marrow biopsy. Now, these gene mutations are not generally things that we're born with. They are things that we acquire as we get older and so an MDS diagnosis is made when at least one of these is found in the bone marrow. Like Amy said when blasts make up more than five percent of the

bone marrow cells, when there are changes to the structure or the form of the bone marrow and the chromosomes can help. About half of MDS patients have abnormal bone marrow chromosomes and so those chromosome abnormalities can be that there are too few chromosomes, too many chromosomes, chromosomes are missing parts or extra parts. They're also... they're bizarre looking chromosomes and they can help both with the diagnosis and they can help also with predicting the prognosis. So, the chance of this getting better or the chance of getting cured and so our bone marrow this is a little cartoon having a bone marrow biopsy. They can either do it lying on the side or with the patient lying on their stomach. A small needle goes in and you get a piece of bone marrow and then this little yellow guy looks at it, the pathologist.

And so I mentioned chromosomes. So, what are chromosomes? Chromosomes are in almost for all intents and purposes all of our cells in our body have chromosomes. We have 23 pairs of chromosomes and that's normal. They're numbered one through 22 and the 23rd are the pair of sex chromosomes. So, if you're a man you have an XY and if you're a female you have two X chromosomes and so chromosomes contain all the genes in the body. So, they determine our genetic makeup, how tall or in my case short we are, color of the eyes, hair and all of that. They come in pairs. The chromosomes copy... the cells copy their genes and then the cell divides and one chromosome makes two chromosomes and so two new identical cells are made. So in this case these two are not identical. So, this is a healthy boy. So, he's got 23 pairs with an XY so everybody's happy. This little guy we can't really tell what it is and the chromosomes are all messed up. He's got too many of everything and so in MDS and in other blood cancers and tumors the chromosomes can be abnormal and in MDS about half of patients with the most common chromosome test about half of the patients with MDS have abnormal chromosomes. So, it's not like we were born with those abnormalities. Those abnormalities were acquired during our lifetime. So, for example, children with Down syndrome have an extra chromosome 21. That's called Trisomy 21, but they were born with that. So, someone with MDS may have Trisomy 21, but they don't have Down syndrome. That's an acquired chromosome abnormality and so these abnormalities can help us both to diagnose the MDS and also to determine what the prognosis of the MDS will be.

So, MDS classification. Historically, there was something called the French-American-British classification of MDS and it was based on the appearance of the bone marrow and the blood cells and so there are groups. There's one called refractory anemia, refractory anemia with excess blasts. That's when the blasts are increased, excess blasts in transformation. That's when it's almost the acute leukemia state and then there was another disorder called CMML. That's now a separate disorder. So, recently the World Health Organization reclassified all these diseases and said we want to classify them more based on not just how they look, but on the chromosome abnormalities and pretty soon they will have the genetic... the gene mutations as part of that as well.

Any questions so far?

Amelia Langston, MD: So, if the World Health Organization and the FAB classifications tell us what we name different stages of MDS it's really the International Prognostic Scoring System or the so called IPSS that allows us to prognosticate a little bit about how a patient is likely to do and the system in most common use today is called the IPSS-R or the Revised IPSS scoring system and basically what this does is it takes into account the percentage of those blast cells that we talked about in the marrow, the specifics of the chromosome abnormalities that are present in the bone marrow and the types of blood cells that are decreased. So, do you have just one lineage down or do you have two lineages or all three lineages that are deficient and how low the numbers are and so using this scoring system which is basically a point system we're able to sub classify patients into really five different prognostic groups that have very different expectations both in terms of survival and risk of development of MDS and just to show you this graphically these are really outcomes based on the revised IPSS category and these are what we call Kaplan Meier curves. So, you start at 100 percent with 100 percent of people living and then following people over time how likely are people in each of those different categories to still be alive and alive and without AML. So, as you can tell there's a very big difference between those patients who have the most favorable risk profile versus the patients that have the most unfavorable risk profile and that helps us as physicians to sort of think about how aggressive we want to be with an individual patient at a given point in time based on how likely it is that they're going to start to have life threatening problems. Now, Martha already alluded to the fact that there are also gene mutations that we can identify by DNA testing and this, again, is another one of those Kaplan Meier curves that really gives you an idea that looking at this particular panel of genes which was described a few years ago, patients who have a mutation in one of these genes have a distinctly less favorable prognosis than patients who have no mutations in any of these genes and we can go on to actually pick from this panel of genes ones that have particularly unfavorable prognoses independent of the IPSS classification or the FAB and this classification system which I think will come into common usage pretty soon just parses things out based on high risk versus intermediate risk versus low risk on the IPSS coupled with information about mutations and what you can see here is that the mutations, the presence or absence of mutations does inform us, does add information independent of sort of what we see under the microscope and in the blood counts.

Martha Arellano, MD: And so some facts about treatment planning in MDS. So, a person that has MDS is usually treated by a hematologist or oncologist. We really suggest that everyone with MDS really consult with a MDS expert because it's such a rare disease and there are so many nuances of the treatment that at some point I think it would be beneficial to see an MDS expert. Talk to the doctor and ask questions about how they want to treat the MDS and about why. So, I'm not saying be belligerent with your doctor, but I think it's important to understand why things are being recommended.

So, what are the goals of treatment in MDS? One, the main one is to either stop or slow down the progression of MDS to acute leukemia. Acute leukemia after MDS is much, much harder to control and treat and so that's one of the goals. Second is to improve the blood counts, suppress

the abnormal cells and to maintain or improve the patient's quality of life and that really can't be minimized because you live with this every day. You want to make sure that you have a good quality of life.

So, in deciding on a treatment the hematologist oncologist will consider who is the patient. Are there other medical problems that the person has? How is their overall health? What is the major problem for the patient? So, is it just anemia because if it's only anemia and not the blasts that are out of control then the treatment plan will target getting rid of that anemia. If it's thrombocytopenia or low platelets then the treatment will be to improve the platelets, etc. If it's all the counts being low then that requires more treatment and then the type and prognostic risk score of the MDS. So, whether it's very low risk or low risk MDS versus whether it's high risk MDS. Those two will require a different approach of treatment.

And so some of the goals for the low risk patients are to decrease the number of blood transfusions that are needed, to decrease the number of platelet transfusions that are necessary, to lower the risk of infection and to increase the number of good quality years of life. Some of the goals for the high risk patients are the same as the low risk patients generally speaking, but also to increase the life expectancy because the life expectancy is much shorter as you've seen from those curves from those survival curves that Amy showed is much shorter than those with the low risk patients and some patients can be cured with a donor of bone marrow transplant.

So, the most common treatments for MDS include observation of the blood counts. So, no treatment, a watch and wait and that's appropriate for some MDS patients. It makes people nervous to have a disease that is probably a cancer and my doctor doesn't want to do anything, but that approach is appropriate for some of the patients with MDS. Transfusion of either red cells or platelets to control the symptoms. Iron chelation to prevent iron buildup from the red cell transfusions. Growth factors. Usually a red cell growth factors but rarely we also use white blood cell growth factors and then there's drug therapy, chemotherapy, clinical trials and stem cell transplantation and so Amy is going to start out with the transplant.

Amelia Langston, MD: So, given that transplantation is the only potentially curative therapy for MDS the first question I always ask myself when see a new patient with MDS is is the patient a transplant candidate and if so how would I do the transplant and when would I do the transplant? In general, we consider patients who are otherwise healthy up to and into their mid-70s and this is a common misconception even among hematologist oncologists is that a patient over the age of, say, 65 is too old to have a transplant. That in today's world that is not the case if the person is otherwise healthy and has a reasonable performance status and I use as kind of a general rule can the patient walk a mile and as sort of a general performance test.

So, who is a transplant candidate? How do transplant doctors think about that? Well, an important tool that we use is a, again, another one of these point systems called the Hematopoietic Cell Transplant Comorbidity Index and what this is is it's really a measure of

general health and most of this reflects historical things like do you have diabetes? Have you had heart problems? Lung problems? Things like that. Some of the things on this list require specialized testing that is done as part of a formal pre-transplant evaluation, but we can get a pretty good idea of a person's candidacy for transplantation particularly when a person is in the older part of the age spectrum. We don't want you to have very many points because we know that the more points you have the more likely it is that you will have serious problems surrounding the transplant maneuver and the more likely it is that you will have life threatening complications of a transplant.

So, what is a transplant? Well, it's really our most powerful but also our most dangerous treatment for blood cancers in general and what we're doing in a transplant is we're using chemotherapy sometimes coupled with radiation therapy to destroy both the diseased marrow as well as the patient's immune system and then we infuse donor cells that will reconstitute both the marrow and also the immune system. Now, what this means because we've transferred the immune system from one person to another is that long term immune suppression is necessary much the same way as if somebody has a kidney transplant or a heart transplant. You have to take medicines to prevent complications. The difference here though that a kidney transplant or a heart transplant patient has to be on those medicines for life. A stem cell transplant patient does not because eventually what happens is that those donor immune cells are reeducated in the immune system of the patient and at that point they become the patient's own, but the catch is that that process of adaptation takes time and I can't tell you at the start that it's going to take six months versus six years, but it's typically somewhere in between those two extremes that patients need to stay on immune suppression and during the time that patients are undergoing the transplant and receiving immune suppressive drugs the major problems that we see are graft versus host diseases which is the donor immune system reacting against being in the wrong body and infection as a consequence of the immune incompetence that we create both by doing the transplant and by having to rely on immune suppressive medicines.

So, how actually does an allogeneic transplant work to cure malignant disease? Well, we have the pre-transplant chemotherapy and radiation which is one prong of the approach and that may do the heavy lifting. It may kill 95 – 99 percent of those abnormal cells in the bone marrow, but the critical element here is that we have a donor immune system that's being transplanted as well and it's capable of mopping up those last few malignant cells that are present in the marrow and this is what accounts for the fact that transplant can cure patients that cannot be cured by chemotherapy alone, but it's this donor immune system that, again, also accounts for why this is such a dangerous procedure because this graft versus host disease which occurs when the donor immune system attacks the patient's normal tissues is the most menacing complication that we see.

Now, what does a transplant actually look like? So, this is a diagram that I actually show to students and fellows and things and when I see a new patient in the clinic I actually draw this diagram for them on the board. So, once the patient has passed all their medical tests and we've

decided... found a donor and we've decided to go forward they're admitted to hospital and they receive some form of what we call conditioning which is the preparative chemotherapy and radiation and then on the appointed day which we call day zero they receive the transplant which for all this fuss about the transplant it's like a blood transfusion. It just runs in through the vein like a unit of blood and if we didn't tell you it was something special you wouldn't even know. It's done right in the patient's room. Now, another point that people sometimes ask questions about bone... what's the difference between a bone marrow transplant and a stem cell transplant? Well, all of these transplants are reflective of the transfer of stem cells. It's a matter of where we take them from. If we extract them from the hip bone of the donor we call that a bone marrow transplant. If we extract them from the blood stream of the donor by a process called apheresis then we call that a blood stem cell transplant, but in both cases we're transferring stem cells. It's just a matter of where we get them from. There are somewhat different properties to the products that we get from the hip bones versus the blood, but basically in either case they're doing the same thing. They're going to reconstitute the bone marrow and the immune system. Now what happens as a consequence of the preparative chemotherapy is that there's a period of time, I call it the miserable period, when you feel the effects of that chemotherapy and when the blood counts which may or may not have been normal at the start drop to essentially zero. So, everybody requires blood transfusions, platelet transfusions and antibiotics because those transplanted cells it's like planting seeds in your garden. If you plant seeds in your garden you're not going to go out and see the new flowers the next day and the germination period for the bone marrow and the blood stem cells is between two and three weeks. So, this period of low blood counts typically lasts for a couple of weeks before things start to rise and patients start to feel better and can exit the hospital. So, most people are in the hospital for a period of around three to four weeks. In the aftermath after you get out of the hospital the story is not done because we continue to have to manipulate the immune suppression and the other medications according to how the patient is doing and we have to monitor very carefully for infections in particular infections that normal people don't get because we've got a patient whose bone marrow has been destroyed and is growing in very slowly and we're actively suppressing the immune system. So, we have to do very specialized monitoring that can only be done in the transplant center which is why when some part of the package of having a transplant is that we need a patient to be immediately accessible to us for at least three to four months surrounding the transplant. So, when you go home if you live in Savannah, you're not going to be going home to Savannah right out of the hospital. You're going to be going to some sort of a halfway house for a while so that we can monitor things and make sure that everything's on track.

Now, there are a number of changes in transplantation that have made this an option for more patients. Certainly one of the big things is better general medical management of a lot of different disorders, but I would say the advances in cardiovascular medicine are probably the single biggest impact. In other words, we have people who 20 years ago would have died of heart disease that are now living on to get blood disorders and we're able to do things like transplants on those patients. We also have over the last 15 or 20 years developed less intensive pre-transplant chemotherapy regimens that... the so called mini transplants that allow us to offer

transplants to patients are older, patients who are somewhat infirm or patients who have had other kinds of aggressive therapies that would have previously precluded undergoing a transplant. We also have better immune suppressive medicines, better supportive care and most recently we've developed new methods of doing transplants that allow successful transplantation even in patients who don't have a fully matched donor and this has been a huge breakthrough because it used to be that people really had to have a match in order for there to be a high likelihood of success, but now we can take patients who have a half matched donor from their family or a mismatched donor from the registry and have a reasonable likelihood that that transplant will go okay.

Now, how do we decide when to transplant and the answer is that I take a transplanter I take this very seriously because what we're doing can produce life threatening complications. So, in thinking about how and when we pull that trigger I really seriously consider does this patient have an immediately life threatening problem? So, we look at the IPSS classification, what's the prognosis of the patient both short term and long term, what are their transfusion requirements, what's their quality of life and how are they responding to medical therapies, what's the blast percentage which gives us an idea of how close they are to becoming leukemic, what are the genetics because that's certainly very informative of what's likely to happen to the patient and finally what is the patient want? Does the patient want that cure at all costs? Is that patient willing to accept the very real risks of the transplant maneuver?

And now I'm going to turn things over to Martha to talk about non-transplant therapy.

Martha Arellano, MD: So, I don't know if people need to stretch their legs for a minute. No? Okay.

Amelia Langston, MD: Do people have questions about what we've talked about so far?

Martha Arellano, MD: Yes, ma'am?

Q3: I was wondering about the (inaudible 45:29) 10 better?

Amelia Langston, MD: So, when we talk about 10 out of 10, nine out of 10, eight out of 10 we're referring to how closely matched the donor and the recipient are and we look at five genes each of which we have two copies of and that's the 10. So, if you're 10 out of 10 match that means that to the extent in terms of the things (inaudible 45:58) 9 out of 10 is a little bit less well matched, eight out of 10 (inaudible 46:09) to say you actually have one chromosome that is exactly the same and the other (inaudible 46:37).

Q4: (inaudible)

Amelia Langston, MD: That's a great question (inaudible 47:00) best place to find a match is going to be in your family (inaudible) and there's a one in four chance that siblings will be HLA matched. If you don't have a family match then the next thing that we do is we go to the registry and there are now about 20 million people registered with the various registries around the world that we can search on. If you are a Caucasian, the odds are actually very good that you can find a match in the range of 80 to 90 percent that you can find a suitable match for transplant. If you are African American or if you are of mixed descent then the (inaudible 47:50) are much lower and that's why for us because we have (inaudible 47:56) proportion of our patients who are African American or of mixed descent. It's been particularly important for us here at Emory that we have these other methods for doing transplants from donors other than perfectly matched donors.

The gentleman in the back I think had a question.

Q5: (inaudible 48:30)

Martha Arellano, MD: I was going to say a lot of what we do is also encourage the community to go to these donor drives and to register as potential donor. So, did that a few years ago.

And so Amy talked about transplant for those... donor transplants for those who are transplant candidates, but what about everyone else – people who are either not candidates or cannot get a transplant. So, the treatment approach the most common treatments include observation or watch and wait which I mentioned, transfusions alone, iron chelation therapy to prevent buildup of iron from all those transfusions, growth factor support using drug therapy, chemotherapy or joining a... signing up for a clinical trial and the right answer if there is a clinical trial then that's the right answer for most cases. When you have a disease where we don't a really, really good chance of cure then a clinical trial is an appropriate option because it will allow us to try to find a better treatment for ourselves and also to improve the care for future patients.

And so let's talk about observation of the blood cell counts or the watch and wait approach. So, watch and wait can be the best option for the low risk patient with MDS. So, the patient that doesn't have life threatening complications so that they don't have severe anemia or low platelets to the point where they're having symptoms and their blast count is not high enough to the point where we think that they're on the verge of progressing to acute leukemia. So, those patients watch and wait is appropriate. It doesn't mean that I tell you hey, you have low risk MDS. I'm going to watch and wait. I'll see you next year. Watch and wait means that we're going to monitor you carefully for a decrease or worsening of your blood counts and also the development of symptoms. So, we want to monitor carefully to make sure that we catch the disease as its progressing before it's too late and so the doctor will monitor the condition, monitor signs and symptoms and the blood counts without initiating any treatment until the treatment is needed. The advantage of this is that patients can avoid the potential side effects of potentially toxic treatment until MDS progresses until the treatment is necessary because these treatments because the only way to cure MDS is with a donor transplant. This treatments are not

curative. So, starting them earlier or before they're needed doesn't really buy us more time. It just means that we spend more time getting treated and so we want to kind of be cognizant of that when we try to decide on treatment. So, people on watch and wait need to continue to see their doctor to have regular tests and physical exams, tell their doctor about any changes or symptoms and understand that treatment may be needed if there are any signs of disease progression.

And so transfusions. So, raise your hand if you've gotten transfusions. So, it's pretty much most people. Right? So, there are two types of transfusions, red cell transfusions and platelet transfusions. There are white cell transfusions are not appropriate. Those are very rare and they only take for a few minutes. So, that's why they're not an option for people with low blood counts. Red cell transfusions improve the red cell count and the hemoglobin and so when we monitor... when I give my patient their little lab report with their blood count results, there's a lot on that report, but I point out I circle the white blood cells, the hemoglobin and the platelets because those are the important things and so the red cell transfusion is done to improve the hemoglobin and to relieve the symptoms of anemia like shortness of breath, dizziness, fatigue, chest pain and things like that. People that have underlying coronary disease, heart disease, may start to have angina due to the anemia and so that's one of the symptoms that we look for. Platelet transfusions will improve the platelet count, but not to the point where they are normal. So, different cancer centers have their own cutoff for platelet transfusions. So, sometimes I'll have patients say at my cancer center they let me go down to 10,000 platelets, but here you want the platelets a little bit higher. So, there's no right or wrong way. The difference is small, but what we... what I do emphasize is that you don't need... we don't need normal platelets to live a normal life. So, we need very few platelets. Hmm. Someone disagrees. So, we need enough platelets to where we're not bleeding spontaneously.

Amelia Langston, MD: (inaudible 54:58) interject that one of the very curious things that I often hear from patients is they'll say I feel so much better after I get my platelet transfusions and that's called the placebo effect. Platelet transfusions do not make you feel better. They help your blood to clot.

Martha Arellano, MD: They prevent and they help the bruising and they prevent the bleeding.

What about iron chelation? So, iron chelation uses medications and they're for the most part pills to remove excess iron and there are several medications that are on the market. They may be appropriate for patients that have anemia who depend on transfusions. So, this is not for the patient that's had one or two units of blood transfused in their lifetime. It's for patients that have a lot of... have had many, many transfusions and they have what we call iron overload. So, too much iron in the blood because that iron can build up in the organs and then cause major problems as well and this is iron chelation...

Yes, ma'am?

Q6: If a patient has had numerous transfusions and is no longer transfusion dependent will the excess iron still remain in the body at that point or will the body take care of it?

Martha Arellano, MD: So, it depends on how much excess there is of iron in the body. So, some of it will dissipate over time, but if they already have iron deposition in the organs then it's likely that they would require a chelation.

Amelia Langston, MD: Now, after a transplant you can actually it's not uncommon that someone you know having in the course of their disease have a lot of blood transfusions and they'd be iron overloaded and if we successfully transplant them often as an alternative to iron chelation we will actually do phlebotomy meaning that we will take blood away because, again, if we can do it that way as opposed to chelation after we fixed the production problem that's almost always preferable.

Martha Arellano, MD: Fewer symptoms.

Amelia Langston, MD: Yes, sir?

Q7: That's something you guys test for anyways every time you test.

Martha Arellano, MD: Mmm hmm. Yeah. The ferritin.

And so it's most appropriate for low risk patients because it takes a long time to bring down the iron to a level where it's acceptable and this is Iron Man in case you didn't know.

So, and so this is some information that was reported on a chelation. So, the outcomes, again, one of these survival curves about patients with true iron overload and the difference whether they were chelated or not chelated and then whether they were adequately chelated. Now, these medications have side effects. So, just prescribing the medicine doesn't bring down the iron. We have to measure compliance whether patients are able to tolerate taking the treatment.

Q8: Are there symptoms to having the overload or do you just have to test for it?

Martha Arellano, MD: So, when generally, and Amy can chime in, when people develop symptoms that's when it's really bad. So, we do test for it. We check the iron panel periodically.

Q8: What would be the symptoms?

Martha Arellano, MD: The iron can build up in the liver causing liver damage, in the worst case scenario liver failure. It can build up in the heart, in the pancreas causing a type of diabetes

and so yeah and then the worse... there are people that are born with too much iron where they absorb too much iron. Their skin changes and gets kind of bronze.

Amelia Langston, MD: By the time you get symptoms you've got (inaudible 59:05)

Q8: You already knew it.

Martha Arellano, MD: Yeah. Yeah, it's pretty bad. Yeah.

And so what about growth factors? Red cell growth factors are generally called... doctors call them ESAs for short, erythropoiesis because the erythropoiesis is the making of red cells stimulating agents or erythropoiesis stimulating factors. They're basically red cell growth factors and there are two on the market and we recommend those. So, for the patient where the main problem is anemia we recommend or where the only problem is anemia we recommend either one of these two drugs. One is given weekly and the other one is given every two to three weeks and it really depends on insurance which one.

Yes, ma'am?

Q9: Why would (inaudible 59:55)

Martha Arellano, MD: So, there are some... there's another one of those risk factors, those scores that we use. We have those for a lot of things, but one of those is we measure the inherent something called erythropoietin. We measure it in the patient and the baseline EPO level, EPO for short, the baseline EPO level can give us an estimation of whether they're going to work or not. So, someone that has a really high EPO level let's say greater than 600 it's unlikely that these agents are going to work. Someone that has a low or normal EPO level is more likely that it's going to work and in the best case scenario someone that has only required a couple of units of blood at all and has a low or normal EPO level their chance of their anemia getting better it's about 70 percent and someone that has a really high EPO level and has required a ton of blood transfusions already their chance is low, around 20 to 30 percent.

Amelia Langston, MD: And sometimes it'll change over time where a patient may start out responding to these erythropoietin agents and then they may stop as their MDS changes and they become sort of unstimulated.

Martha Arellano, MD: Yeah and so when we make these treatment decisions and treatment recommendations they're not final. If you're on Procrit it doesn't mean that you're always going to be on Procrit and that's the only treatment you're ever going to need. As we evaluate things going along will the Procrit no longer works. Well, now we need to go to drug therapy or chemotherapy or we really need to think seriously about whether you can get a transplant or not.

Q10: (inaudible 1:01:50) for a second the iron overload. Is there on the blood test a liver indicator that above a certain count that you can (inaudible 1:02:02) to address the iron level? What is that on the blood test?

Martha Arellano, MD: Normally, on a blood test the liver... there's a liver panel that can be checked, but it doesn't really tell you why... if your liver test is abnormal it doesn't tell you why and it's less likely iron overload generally is fairly rare. So, having a high liver test may be more related to medications than iron overload, but the doctor will check periodically something called a ferritin or an iron panel. I call it the iron panel and so it's not something that we check frequently, but...

Q10: My iron level has gone up to about 1,800, but she said it's okay because the liver looks good.

Martha Arellano, MD: Okay. The ferritin.

Q10: (inaudible 1:02:51) than liver.

Amelia Langston, MD: That's hard to say and I don't know that we should really without knowing...

Martha Arellano, MD: You're into the specifics, but it doesn't really depend on one number of one blood test. It depends on a lot of... the number of transfusions. Someone that's had 200 units of blood probably have iron overload unless they've been losing their blood, that iron.

Anything else?

So, what about white blood cell growth factors? There are two types. This is GCSF usually called Neupogen. These are rarely used. Sometimes for the very low risk patients that did not respond to one of these drugs, Procrit or Aranesp, you can add a little bit of this growth factor and improve the response, but that's these are nuances. That's really when you should see an MDS expert to know because some of these medicines are actually harmful, could be harmful or cause certain side effects when you use them and using them has nuances. Platelet growth factors are not on the market. They're investigational and they don't work that well for MDS. So, it's not sure that there'll ever be an option for MDS.

What about drug therapy? So, there's single drug approaches that are FDA approved for MDS at this point and the main ones are called the hypomethylating agents. The hypomethylating agents there are two types. One is called Vidaza and one is called Dacogen or Azacitidine and Decitabine. They were initially studied for the intermediate and high risk patients, but they're currently used also for the low risk patients when they stop responding to the other treatments.

They can improve the bone marrow function. They can kill the blast cells, the unhealthy cells and they're given either through the vein or under the skin subcutaneously.

A drug called Lenalidomide or... Yes?

Q11: Okay. Before when we found out that he had MDS before we ever came to Winship it was a period of about three months or so they continued to give him Dacogen for, I guess, was it just preventive or was it just to keep him at a level that he needed to be as they worked on getting a donor?

Martha Arellano, MD: And that's... so, the second one. If you have too many of the blasts and you're high risk. So, you have a high risk MDS and we just sit there and wait months for you to get to the transplant doctor, the MDS may continue to progress and so we generally recommend that something be done in the meantime and that's probably why he was getting the Decitabine.

So, Lenalidomide is a drug, it's a pill, that is the preferred therapy for patients with the low risk type of MDS and it works best when the MDS has something called deletion of 5Q. So, five is the fifth chromosome and Q is the long arm. So, people that have an abnormality of the long arm of the fifth chromosome with MDS tend to respond better and these are patients that generally have only anemia and it improves their anemia in a lot of those patients. It can be combined with other treatments and that's usually in clinical trials that they're combining. Imatinib mesylate, Gleevec, is a drug that initially was FDA approved for another condition called CML or chronic myelogenous leukemia and then they found out that it can also work in patients with any blood disorder whether it's MDS or something else that has a specific gene mutation called PDGFR and so it's fairly rare in MDS. So, in my practice I haven't used it for MDS.

Q12: You had (inaudible 1:07:41) Revlimid. If you were transfusion dependent and started Revlimid and magically at three months improved your hemoglobin. From what I've read that'll last about 40 – 41 weeks. The numbers went dramatically up in the hemoglobin. Would they go down very, very fast or would that be a gradual thing when it starts to go down?

Martha Arellano, MD: So, it can happen both ways. Like Amy said these treatments will eventually stop working because they're not treatments that will cure the MDS and so for some people the Revlimid will work for a few weeks, for some people a few months and for rare people it may work longer than months maybe years and when it stops it's usually a gradual problem. You start seeing that you're getting a little bit more anemic and... to the point where you start needing transfusions again, but that's a sign of the drug no longer working. You're welcome.

So, what about combination treatments? Most patients treated with the most powerful drugs, the hypomethylating agents who achieve a response will lose their response over time and the outcome of MDS after these drugs stop working is very poor and so because of that there's a lot

of research being done with combining different drugs until hopefully one day we'll find something that will cure that isn't the transplant. So, clinical trials are and this is when a clinical is a good option if you can find a combination.

Chemotherapy is generally is not a long term option for MDS and it's not a very good option to be honest. It causes a lot of side effects and there are newer chemo type drugs that are in clinical trials currently and generally chemotherapy is reserved for patients who are being prepared to have a donor transplant when the blasts are close to it being acute leukemia and you want to reduce them kind of quickly. Chemo can reduce the blasts quickly, but they come right back. So, you have to do something else after that.

So, how do we try to improve treatments for MDS? What are the tools that we use? We talked about the gene mutations and chromosome abnormalities and these are things... so MDS is a very genetically unstable disease meaning it has a lot of gene mutations, a lot of chromosome abnormalities, but the discovery of all these gene mutations that new information has opened the door to kind of defining what these mutations mean. What happens if this gene is mutated? Let's say IDH1. What happens to the cell when it acquires that type of mutation? How does it allow the MDS to either start or to progress and one of the good things that's come out of understanding the science behind this is that there's the potential for new treatments, for new targeted treatments. So, right now there's a treatment for this IDH mutation. It's in MDS research. It's also in AML. It hopefully will be approved for AML soon. The same for there's also an IDH2 mutation. There is... there's a FLT3 mutation. There's a KIT targeted treatment and there's a JAK2 targeted treatment and these things are all being researched now for MDS.

I'm going to hand it to Amy now.

Amelia Langston, MD: So, what about clinical trials and I think it's important to talk about what actually constitutes a clinical trial and a clinical trial is really a carefully controlled and monitored research study aimed at improving treatment options, improving survival and improving quality of life, but fundamentally what a clinical trial oftentimes does is it gives patients access to promising new therapies that are not otherwise available to them off the shelf, but while offered protection against possible unknown effects through the regulation of the research through what we call IRBs or Institutional Review Boards that monitor... that help us to monitor these trials. Another important thing to understand is that a patient participating in a clinical trial can stop that clinical trial at any time for any reason. So, it's not like you're signing onto something and you have to stay on that clinical trial indefinitely. At any time you can say or we can say I don't think this is in this person's best interest and we shouldn't continue.

Now, trials are not simply for people with the most advanced disease or for people who have failed things. We also have clinical trials that are designed for patients at the early part of their disease. So... and trials can either be testing new treatments or they can be comparing one treatment... one established treatment with another or an established treatment with a new

treatment that's being developed. Now, there's several phases of clinical trials. Phase I clinical trials are those where we have a new agent that has recently been developed and may have only been given to a limited number of people and the purpose of the Phase I trial is to establish a dose of the drug that is well tolerated, that's safe and it is not designed to test efficacy. We're looking for safety and oftentimes for what we call pharmacokinetics and pharmacodynamics meaning are we delivering the drug where we want it to be? Is it doing biochemically what we expect it to as an agent? In Phase II trials we've established a level of... a dosage of the drug that we believe to be safe and we're beginning to explore the efficacy of the drug at that established dose. In Phase III we've had... we're taking a drug that shows promise in the Phase II trial and we are comparing it against some gold standard of care. So, for example, it might be for a patient with aggressive MDS it might be testing a new agent against an agent like Vidaza or Dacogen as asking which is the more efficacious strategy.

Now, there are a number of promising investigational approaches I'll just mention that are currently in clinical trials both here and elsewhere. There's a lot of talk in the press now, but... and in the medical literature about immune therapies for cancer. These are oftentimes but not always used in combination with other agents and they're certainly being explored actively in MDS. There're as Martha already mentioned there are targeted therapies that are specifically aimed at individual genetic mutations. So, if you have a mutation in this gene, we may have a drug that targets specifically that mutation. Another excited area is by specific antibodies which have been they're kind of what I'll call smart bombs that actually direct the immune system to the target cell. Now, what that means is that you've got to have a molecule on the surface or somewhere in that cell that we can use to direct the bomb to the right place, but this is a way to reduce the toxicity of new therapies and reduce the toxicity of the immune system in kind of attacking things willy-nilly and then we have a variety of different combination regimens many of which involve an existing agent in combination with a novel agent.

So, just as an example an immune therapy for AML and MDS we've got a number of different smart bombs, if you will, ranging from antibodies that direct a payload of chemotherapy or other drug to a specific tumor cell target. We have engineered immune cells that have been programmed, if you will, to react against the tumor cell. We have agents called checkpoint inhibitors that essentially take the brakes off the immune system and allow the normal immune system to attack tumor cells. They essentially are restoring the normal immune surveillance that ought to be protecting us against cancer. So, all of these things have at the core of it trying to increase the specificity of our treatments against the tumor cells sparing the normal cells that often get caught in the crossfire with our more conventional therapies. Again, as we have alluded to several times there are a number of different gene mutations for which we have targeted agents already in the clinic. The ones with stars are ones that we already actually have agents that are available for those patients who have mutations in those genes.

So, for many patients a clinical trial can be the best option and a great website that you can go to look at clinical trials across the country is ClinicalTrials.gov which lists all of the different clinical trials that are available in the United States.

Martha Arellano, MD: And so if you go to this website and type in ‘MDS’ then you can go here and say Recruiting. It’ll give you all the studies for MDS that are accepting patients and some of those are international studies and so this website if you do the advanced search will allow you to specify, so I want to find a trial in Georgia for MDS that is newly diagnosed. You can put that in there or for MDS that has relapsed or progressed. You can put that in there, too. So, this is the most comprehensive website where a clinical trial can be found.

Q13: (Inaudible 1:20:45) for MDS.

Martha Arellano, MD: So, currently we had a study with one of those... let’s see. One of this PD1, anti-PD1 treatments and it’s currently not recruiting patients. So, I believe it completed accrual. We don’t have any of these currently open. They’re still in development. So, this is more what the future could look like.

So, what are some of the potential treatment side effects or complications? A lot of these drugs although we want smart medications that can tell a bad cell from a normal cell, we don’t really have those yet. The hypomethylating agents were specifically developed for MDS and considering that most patients with MDS are older than 70. So, they’re very well tolerated. They’re fairly well tolerated. People can have symptoms, but they’re not like what you get with chemotherapy. Chemotherapy is sort of a bomb that is not specific and that wipes out everything that gets in its way including all the blood counts. People get mouth sores. They lose their hair. The risk of infection can increase while all the counts are low. Things like that. Irritation of the mouth and the stomach and the colon, so nausea, vomiting and diarrhea. So, those are side effects that you typically see with regular chemotherapy. The hypomethylating agents tend to not cause that although with that said I had a patient come in and say after about six months on Azacitidine and said, “Hey, you told me I wasn’t going to lose my hair. Look.” So, normally hair loss is not one of the side effects, but every patient is a little bit different.

And so next I’m going to talk about coping about some of the... with some of the side effects of both the MDS and also of the treatment and sort of how to cope with living with MDS and so we tell people judicious hygiene, good handwashing, antibiotics to prevent infection. When patients and this is also a variability among cancer centers based on how many antibiotics you may see. So, I see a patient and they say well, they didn’t tell me to take that specific antibiotic. Is that doctor wrong? I tell them no. There isn’t one way to do this. So, there is some variability and there are some areas where there is no right answer. So, I tell them this antibiotic is really no different than that other antibiotic and antibiotics are only given to people that are severely neutropenic meaning the good white blood cells, the neutrophils that fight infection are extremely low for a long period of time. Medications for nausea, vomiting, good handwashing to

prevent infection, keeping... if you have a catheter, a central line or a port keeping that clean, practicing good dental hygiene.

Being active. So, patients... I had several patients generally if I send my patient to Amy I kind of have to build them up before she sees them because she might do the eyeball test and say hey, you don't look like you can walk a mile. Go back to Martha. Have her fix you up. So, come back. So, I tell my patients that being active is very important. Stay active. So, don't act sick. Keep doing your thing, but I have this disease. Yes, but the disease doesn't have you. So... Right? So, these are the things that you can do to help. Stay active, do as much of your self-care as possible. Someone else can do the dishes, but you can do your own stuff. Take daily walks. If you can do more than walk if you can go for runs have at it. Balance activity with rest. If the neutrophils are very low try to stay away from crowds and gardening. This is one of the tough things... tough conversations with my patients who love play in the dirt. It's like your neutrophils are too low. They're 100, so I'm going to ask you not to play in the dirt anymore and that's because I want to protect you from infection.

What about diet? So, people ask should I restrict my diet. Should I avoid certain foods and I tell them to eat a normal healthy balanced diet. Sometimes when we have this diseases we start eating only comfort foods and then we kind of forget and as doctors sometimes we also forget that there are other things that can happen when all you eat are cheeseburgers and French fries. So, try to eat a good balanced diet.

What about intimacy or our sex life? What does that look like with MDS? I had a patient that actually is doing very well, went to transplant, but when I saw him, I'm a hugger. So, I gave him a hug and his wife looked at me and said, "You know, why did you give him a hug? We were told never to hug because that can cause infection," and so I almost cried. I'm like oh, my gosh. Said you're his doctor. We don't see you that much. I see him every day and I can't hug him. What gives? And I didn't realize that they had been told that. Two years previously. So, I'm like you're telling me you haven't hugged your husband. You guys haven't been intimate for two years because someone said you could catch an infection? And that was the case and so I bring this up because people don't bring it up. They're embarrassed or whatever. So, I think it's important because I don't want to be the only one giving out hugs. So, it's a part of life. Sex and intimacy, they're a normal part of life. There are no special limits. Just use caution especially if the platelets are low below 20,000 or 10,000. Patients and their partners of reproductive age should avoid getting pregnant while taking chemotherapy. That's for MDS population that's not usually an issue because medications can harm the fetus. Tell your doctor or healthcare team if you're having problems with a low sex drive or erectile dysfunction because there may be... You know, that's part of what we do as well when we see these patients and Amy same thing. When she transplants a patient she becomes their primary care doctor for that period of time. I have a patient with MDS and I'm giving them all these medications, many of them that could potentially have drug interactions with something else that someone else may give them. I kind of become their primary doctor and so I'll ask you about these things, but if I don't tell me, tell

your doctor we have this problem. You want to... you told me that the treatment is going to improve my quality of life but my quality life is terrible because of this or that. So, I think those things are important to mention.

What about depression? Being depressed... depression is very common in our patient population and it's another thing that people don't mention and so we ask... we have that sheet in the clinic that people fill out with their symptoms, but I think it's important to bring it up. So, don't expect someone to just read that and react to it. Being depressed can keep you from doing what's important. It can cause you to have also symptoms, aches and pains, not sleep, be anxious and that can kind of get in the way of normal life. It can best be... some patients in my experience my patients say I already take enough pills. I don't want to take any more pills, but talking therapy can be very helpful in that case as well and so it's important to bring that up.

Then in terms of follow up. So, kind of be in charge of your own care. I can tell based on the fact that you're here that you are that population of people that want to take charge and that are in charge of their own care. So, track each visit, record what's discussed. I give my patients their report. So, if they had a bone marrow biopsy I give them their report to take back to their doctor, their blood counts. Ask the doctor why something is being done and what to expect. Discuss results. Find out what else is needed for follow up and seek medical and psychological support for those things that can happen and a second opinion is appropriate for most patients and I don't... Patients ask me... even my own patients may go somewhere else for a second opinion and they hesitate because they don't want to hurt my feelings and I tell them, you know, it's not about me and my feelings. My feelings are not hurt. I actually expect my patients to seek a second opinion because I want them to get the best treatment possible.

And that's Amy.

Amelia Langston, MD: This is a picture of Robin Roberts who I think has probably singlehandedly done more to increase the public awareness of MDS than probably anyone else that I can think of. She as many of you know had breast cancer, received chemotherapy and had secondary MDS as a consequence of that chemotherapy for her breast cancer. She subsequently underwent a transplant from her sister and is doing great and back on TV and living a normal life.

So, what that really I think that's really all we had to present. We wanted to really open things up for questions, comments, stories, discussion.

Yes, ma'am?

Q14: You talk about finding a hematologist that specializes in MDS. I know that we (inaudible 1:33:01) local (inaudible) originally diagnosed with MDS (inaudible) consulted with Emory for

(inaudible) transplant (inaudible). How do you find a hematologist that specializes in MDS and what does that mean?

Amelia Langston, MD: Well, that's a great question and I think that it sounds like you already have if you've been here for a consultation because really what we're talking about is going to an academic center where you see a person that what they do is they take care of blood cancers and they tend to be a little bit more familiar with the nuance of not only therapy but also sometimes parsing out the diagnosis. It also gives you access to skilled hematopathologists to review the slides that form the basis for the diagnosis because there are people that I have seen who were labeled as MDS and we came to find upon testing that they actually didn't have MDS. They had a different problem altogether. So, I think having at least a consultation at an academic center is really what we're talking about.

Martha Arellano, MD: And I think how you get there your doctor may already be able to refer you or people like the MDS Foundation they have a list of MDS providers registered on their website. They can also... and they have people that can help decide where to go.

Amelia Langston, MD: And I want to emphasize that although we've sort of done this Mutt and Jeff show with me as the transplanter and Martha as the sort of disease management person. In fact, we both have a primary interest in MDS and we both have both transplant and non-transplant MDS patients.

So, yes?

Q15: (Inaudible 1:35:14) that all hematology oncologists from Emory should be MDS specialists or experts.

Amelia Langston, MD: No, not necessarily. There are certain doctors here. So, when a person is referred in and I can't speak to how this works at other centers, but when a person is referred or self-refers here and they state their diagnosis they are going to be directed toward a disease expert in their field. So, you would not be placed in my clinic if you had lung cancer because I'm not a lung cancer disease expert, but if you have MDS most likely you're going to be assigned to either my clinic or Martha's clinic because we're kind of the MDS point people.

Q16: (Inaudible 1:36:10) five years ago (inaudible) an oncologist hematologist at Emory and then it has turned into MDS are we in the right place?

Amelia Langston, MD: Yes.

Martha Arellano, MD: So, I have patients in my clinic from my colleague next door who treats lung cancer or breast cancer. So, they just make an internal referral. Now, there are physicians... we're not the only ones that would treat MDS. There are a few other physicians.

Amelia Langston, MD: But it's a limited panel of people.

Martha Arellano, MD: It's small. So, say if you started out with, I don't know, Dr. Heffner, he can also manage MDS.

Q17: My question is after being diagnosed with MDS it seems like my autoimmune system is imploding in upon itself. Is that as a result of the MDS or is that a separate issue altogether and when I say autoimmune system imploding it's things like Sjogren's and antiphospholipid syndrome and antigens for something being off the chart and there being a concern. Those types of things have arisen.

Amelia Langston, MD: Well, and again I think it's always dangerous for us without all the medical information to really comment on someone's specific medical problems, but MDS can have a... its roots in an autoimmune sort of picture and there is a subset of MDS patients where their MDS is actually caused by autoimmunity. It's not usually associated with the type of autoimmunity that you're describing. So, it may be two separate things.

Q18: Going back to one of your previous charts, I'm sure I misunderstood it. Okay? You're talking about treatments and Vidaza and at some point the chart seemed to say that if the Vidaza quit working you were going to die in four months. I misread that?

Martha Arellano, MD: Not four months, but the... I think you're right in that the prognosis on MDS when the Vidaza stops working is poor. It's not as good as when you started out or when you're responding to treatment.

Amelia Langston, MD: Just to build upon that what we're really talking about in terms of the poor prognosis of MDS having failed Vidaza or Dacogen is patients specifically with high grade MDS. So, there's a whole other group of people that may be on Vidaza or Dacogen primarily because of symptomatic anemia and those patients don't have the same unfavorable prognosis but the people that are on their way to AML and that's why they were on the Vidaza or Dacogen. Once those people stop responding they tend to have a relatively unfavorable prognosis.

Martha Arellano, MD: And the high blasts. The high blasts.

Amelia Langston, MD: But anybody that tells you you got X number of months to live that's just silly.

Q18: Low risk situation.

Amelia Langston, MD: Low risk situation, different deal. Different ballgame.

Yes, sir.

Q19: Is there really any other drug other than Vidaza to treat the basic symptoms right now unless you do a transplant which I'm too old for.

Amelia Langston, MD: There is a subset of patients that will respond to the Revlimid, the Lenalidomide but other than that we don't have good off the shelf options.

Q20: One of the charts you had earlier was the age that people tend to get MDS. I was like in one of those categories that was in between that you guys didn't mention. Early 50s. Is that something I might be able to look forward to having in my 70s or older even though I had a transplant and the MDS doesn't show up anymore just because in my case my brother who was the donor might get it when he's in his 70s?

Amelia Langston, MD: Well, anytime we do a transplant from one person to another if there is something wrong with the marrow of the person who was the donor the recipient can subsequently get that problem, but I don't think we're talking... you're not such an outlier that I'm real worried about that.

Q20: So, it's not like I'm... if you've had it once it's not like you're going to get it again?

Amelia Langston, MD: No.

Comments? Yes, sir?

Q21: I have a (inaudible 1:41:51) for a transplant back in April and the week before we did the transplant the Revlimid started working. So, we have put it off. My brother is my donor. He's a 10 for 10. Is there some way to go ahead and get his stem cells in case something happens to him for that time when I need the transplant?

Martha Arellano, MD: Before he starts misbehaving?

Q21: You never know what he's going to do.

Amelia Langston, MD: It's very rare that we consider doing that for several reasons. One, we don't necessarily know that a person's ever going really go to a transplant. We would prefer to use a fresh product as opposed to a frozen product and so generally we don't do that unless there is... or some sort of extenuating circumstance as such that we really believe that we might not have access to the donor again. So, for example I've had occasional donors where we had to get them out of foreign countries or something where there was the possibility they might not be able to ever come back, but I'd say that's very, very rare circumstance.

Martha Arellano, MD: But I'm glad the Revlimid is working.

Amelia Langston, MD: Yes. As long as you can delay having to take those risks of the transplant we're all about that.

Q22: I had a question just out of curiosity's sake that (inaudible 1:43:30).

Amelia Langston, MD: That's a great question. So, the success of the transplant depends on a lot of different factors. It depends on the state of affairs of the bone marrow at the time the patient goes into the transplant, how many blasts are in the marrow, how extensive the prior therapy has been. It depends on the general health of the patient. It depends on who the donor is and how closely matched they are and a variety of other factors that we don't know until we evaluate the patient, but just to put it sort of in some sort of a framework in the best of circumstances if we have a healthy patient who has a perfectly matched donor who does not have excess blasts at the time of transplant we can be looking at about a 60 percent chance of long term cure. Okay? On the other hand if we've got a patient that's on the verge of leukemia or who has other strikes against them we're looking at a less favorable outlook. So, what we want is to have the disease controlled at the time of transplant and to have the healthiest and fittest patient and the best donor.

Q23: When you say long term (inaudible 1:45:12)?

Amelia Langston, MD: Well generally if the MDS is going to come back it comes back typically within five years and so we're looking at that kind of a horizon in terms of relapse. The other thing to understand, again, in terms of full disclosure is that independent of relapse patients who undergo transplant do not have quite the same life expectancy as an age matched person because of the wear and tear on the body that is done in the course of the transplant and so secondary cancers become a concern, late organ toxicities become a concern and what that means and what I say to my patients upfront is when you leave me at five years or six years or seven years or whenever you have got to have a good doctor that's going to do aggressive surveillance for the kinds of problems that come up in post-transplant patients.

Martha Arellano, MD: Heart disease and all those high cholesterol, things like that.

Amelia Langston, MD: And the normal cancers that arise in people in your age range. The other thing that I very strongly recommend to all of my patients who have had transplant is that they have a good dermatologist that monitors them with a full body exam every... at least once a year because of the different types of secondary cancers that occur after transplant more than half of them are skin cancers that can be managed if they're seen... if they're picked up early.

Martha Arellano, MD: That's because of the immune system being suppressed. The five year number is what's used as a standard for all cancer where we determine cure even though that number's not... it's just kind a random number that was chosen.

Amelia Langston, MD: Other things people want to talk about? Great. Well, thank you for being here.

Sara M. Tinsley: Hi, everybody. I'm Sara. Feel free to keep eating. If you have questions, please interrupt me. I'm a nurse practitioner that works at Moffitt Cancer in Tampa, Florida and I'm so thrilled to be here. This is my favorite type of presentation or interactive arena for talking to patients and their family members, their support system, on really educating about Myelodysplastic Syndrome, but also helping you try to problem solve about how do you kind of normalize it and make it part of who you are without letting the disease define you, but you define the disease. Right?

So, we have *Building Blocks of Hope* at the MDS Foundation. Have you all used that? Have you found that? What do you think about it? Easy to understand, easy to use? Very good. Of course, I'm asking everybody while they're eating. Right? So, and helping you, the *Patient and Caregiver Guide for Living with MDS*. Really, we're focusing on living not letting it define us and get so focused on oh, my goodness if I have high risk disease does this mean I'm going to die in a couple years? Is this really what it's going to look like but really focus on living and adapting to having Myelodysplastic Syndrome and if many of you have had the challenge of explaining it to your family members or friends it's hard to explain something like Myelodysplastic Syndrome. It's hard enough to pronounce, but then to try to explain it to your friends and family members. So, hopefully by attending this meeting you'll be better equipped to handle those type of questions that come and the explanations to your friends and family.

So, when to start treatment. You heard this presented very nicely this morning and remember we think of Myelodysplastic Syndrome in two big buckets – low risk disease and high risk disease, and so we think about that like the goals of treatment depend on whether you have low risk disease or high risk disease. So, that's one of the piece of information that you really want to take away from this meeting is being able to discuss whether you have low risk disease or high risk disease with whoever your hematologist is, but these are treatment triggers that we look at and I do have an independent clinic. I see lots and lots of MDS patients that doctors that come up with the treatment then send them to me to help explain the disease and how patients get through their treatments and to administer the transfusions and watch for iron overload. So, when a person starts to need transfusions with packed red blood cells or platelets regularly then that can be a trigger for when you need to start treatment. Remember we talked about observation. That's a reasonable approach to many patients who have lower risk disease is just observing you, having you come in regularly to check your CBC or complete blood cell count and see if it's stable, but when you start to need transfusions or you start to have progressive or symptomatic cytopenias.

What does that mean to you? Anybody. Progressive or symptomatic cytopenias. Does that mean anything to you?

Q24: There's no (inaudible 1:52:10) and you start to have that build on each other into what may seem one thing is actually when you build up to something else. Its symptoms that might not seem like it's one thing, but when you start adding different symptoms together and it builds up it might send you in different direction where your doctor or health professional needs to more customize your treatment to just help fight the disease.

Sara M. Tinsley: To help you to have a better quality of life. So, symptomatic cytopenias... Thank you that was excellent. Symptomatic cytopenias is meaning cytopenias or lowering of blood counts. So, if you start needing transfusions you may have started out needing packed red blood cell transfusions maybe once a month or once every other month and then you start needing them every three weeks and then every two weeks. That is a progressive cytopenias or having low platelet count. How many people have had problems with low platelets? Yes. So, a fair number with low platelets and a normal platelet count is usually like 143,000 to 400,000. That's a big range and you can do well without a platelet transfusion even when your platelets get to 50 you can still do pretty good, but when you start having bleeding and you're less than 50 then you can run into problems. Normally, we transfuse platelets at our institution if you're 10,000 or less because you can have spontaneous bleeding, but if you're bleeding and you're 50,000 or less then you would get a platelet transfusion. So, those are reasons to start treatment. We also talked about blasts this morning, leukemic like blasts. These are really immature cells that as they increase then that's a sign that your disease is getting worse. You don't want to see increased blasts in your bloodwork on that CBC. When you do a differential the differential tells you what type of cells you have. So, if you see the blast percentage increasing then that's a sign that things are getting worse and then just high risk disease in generally. Remember our high risk disease patients are more likely or individuals are more likely to progress to AML. So, you want to start therapy for high risk disease to prevent them from changing into acute myeloid leukemia and then you really want to look at the patient individually. This comes up a lot about older patients. It depends on really age is just a number and so an older patient really is defined by that whether it's not really just 60 or older or 70 or older or 80 or older it's what is their performance status look like and what does performance status mean? Are you able to do your normal activities? Can you get up and get dressed and get bathed and go about your normal daily activities without having significant problems? That's what we're talking about with performance status. Comorbidities is your other illnesses and then the IPSS-R we're looking at your risk category. With lower risk disease we're trying to improve hematopoiesis which means improve your bone marrow's ability to make your normal functioning blood counts. So, when we treat lower risk disease to try to decrease transfusion dependence you're really looking at can you decrease the number of transfusions that person gets and improve their neutrophils to keep them from getting an infection or improve their platelet count and then for higher risk disease we're trying to help patients live longer by keeping them from changing into acute myelogenous leukemia because we know once that happens then a person's really in trouble and then

cytogenetic status, deletion 5Q is a favorable subtype and complex cytogenetics. Is that a term you all are familiar with? Complex cytogenetics? So, remember how we were talking about the chromosomes how you can have deletions and insertions and translocations and all extra copies of chromosomes. So, when you have three or more chromosome abnormalities that automatically makes you higher risk disease and that can change over time. So, what you start with on your MDS journey can change when they repeat your bone marrow biopsy. So, that's one of the things you really need to be able to tell what your IPSS Revised is because we look at those cytogenetics and then lifestyle and personal choice.

So, does anybody have questions about all of these things? No. Does anybody have something they want to add? How many of you know what your cytogenetic abnormalities are? I know somebody does and you have 5Q-. So, you have 46XX. Right? So, that's normal chromosomes for a female. Anybody else?

Q25: I know that I don't have the 5Q or deleted 5Q.

Sara M. Tinsley: You don't have deletion 5Q and do you know if yours is normal like for a male or...?

Q25: I don't.

Sara M. Tinsley: And what about mutation profiles? Does anybody know what type of mutations you have? So, those are some questions you could ask if they've ever checked a mutation profile and what your chromosomes look like just so you can learn about your own disease. Anything else? No.

And remember we're presenting a lot of information today and so the expectation is not that you go home and you'll remember everything, but if you can take away key pieces that helps you understand your disease better and helps you manage your life better then we've done a lot. We've helped you.

So, we talked about this this morning also. Allogeneic bone marrow transplant is the only potential cure for Myelodysplastic Syndrome, but it's not an option for many individuals. You have to have either an HLA identical donor or you have to have be of the age that they would accept you for transplant and they also look at your comorbidities. Comorbidities means what other illnesses you have as to whether transplant is an option for you and we think that age alone should not exclude you from any of the active therapies and remember it takes time for all of our treatments for Myelodysplastic Syndrome to work. Usually four to six months of therapy. So, this is not a sprint. It's more like a marathon and patience is really helpful. It takes time to work and it doesn't work indefinitely. There's usually amount of time that is expected that it's going to work and you'll be monitored along the course of your treatment to see when you start to lose

your response. So, what do you think one of the ways you would be able to tell if you were on a treatment that's working that it's stopped working? What about with your Revlimid treatment?

Q26: Well, (inaudible 2:01:41)

Sara M. Tinsley: You had symptoms of fatigue before and what about your hemoglobin?

Q26: (inaudible 2:01:48)

Sara M. Tinsley: You didn't have it before and now you have a normal hemoglobin. Right? So, one of the ways you would know you're losing your response is if your hemoglobin stops dropping. Many of you may know that when you treat with Revlimid if it's working the red blood cell count goes up, hemoglobin improves, but the neutrophils can go lower and the platelets can go lower. So, you just have to monitor that, but the reds to where they become... you don't need transfusions anymore and then blood counts often get worse before they get better when you start any of these treatments, Azacitidine, Decitabine, Lenalidomide or Revlimid, during the first couple of months of treatment things get worse. So, that doesn't mean you're failing. It just takes time for these to work. Usually four to six months. How long did it take...? I know you said you started to respond, so you didn't go to transplant.

Q27: (inaudible 2:02:50)

Sara M. Tinsley: It took eight weeks. So, there you go. His was soon, a quick response. So, that's great.

And then you want to really proactively manage any potential side effects to minimize them. Some of the symptoms we see with Azacitidine. Have any of you been treated with that or Decitabine? Yes, no... Yes? What kind of side effects did you have?

Q28: (inaudible 2:03:17) a lot. (Inaudible)

Sara M. Tinsley: Constipation.

Q29: A weakness, can't remember everything. I got dehydrated real easily. Diarrhea.

Sara M. Tinsley: Right. Yes. You had...?

Q30: I had a (inaudible 2:03:38)

Sara M. Tinsley: Your teeth were hurting.

Q30: Yes. Only when I (inaudible 2:03:44)

Sara M. Tinsley: Okay. So, some teeth pain. Constipation is a very common side effect with Azacitidine or Vidaza and one of the things you can do when you start to get treated is start to take something to loosen up your bowels so that you don't end up a week without a bowel movement. So, you really want to monitor that. Also if you get it... it can be given as an injection or it can be given IV. If you get it as an injection it can cause injection site reaction. So, monitoring for that, the type of reactions you have when you get a shot and then letting your healthcare team know if it's getting redder and more painful.

So, why does it take time for these treatments to work? As your blood counts drop as MDS progresses your normal blood counts are crowded out by these abnormal cells in your bone marrow and in your blood. On the right this is looking at the neutrophil count, absolute neutrophil count. Remember this is a type of cell that's a white blood cell that really tells what your risk of infection is. So, when your neutrophils are less than 1,000 then you're at increased risk for infection. So, this graph, this bar, shows you 3.2 which is like a normal neutrophil count, but with the first... as the disease progresses as MDS progresses or with these treatments the neutrophil count can drop low and this is where the person is at risk for infection and as you begin to respond to treatment the bone marrow begins to recover and it allows your bone marrow to make more healthy blood cells and then the blood count should rise up and these are weeks of treatment down here and then should improve over time. So, it's cleaning it out and as the response continues you can be weaned from the frequency of getting your blood counts checked and hopefully getting transfusions or needing any... if you are put on preventative antibiotics if your neutrophil count recovers you can come off of those preventive antibiotics or if you are needing platelet transfusions that's one of the things that could be stopped as you're having a response and your platelets are back into the normal range or if they're above that 50 and no signs of bleeding, but really what's challenging is getting through the first couple of cycles because it can be discouraging if you're having lower blood counts you're needing more frequent transfusions, you're having neutropenia and having to be concerned about having an infection or needing platelet transfusions, but really you don't want to have your therapy stopped too soon because you'll never be able to see if you're going to have a response if you don't get to that four to six months of treatment.

So, time is required for your best response. Again, a minimum of four to six months. It gets worse before it gets better and then just to be aware that it works over time so that you don't give up which is hard because I think it's hard to stick in there when you don't feel well and be hopeful when you don't know for sure if you're going to respond.

This is a graph of someone who had trilineage response. Trilineage means in your bone marrow you make white blood cells, red blood cells and platelets and this is really graphing those out of a real patient. You can see the hemoglobin in pink here, this pink bar, and then the hemoglobin started at 12 and then dipped down to eight and then this is the first cycle. So, probably transfusions here and here and then out here at cycle four you can see how it came up and stayed

up and then this is your white blood cell count, 1,000, and you can see how that went up and stayed up and then the platelet count here is this yellow bar and you can see how the platelets were really low and the platelets are over here. So, this is 20, 40, 60,000, 80,000, 100,000 and remember we said 140 usually to 400,000 is normal. So, this is still not a normal platelet count, but you can see it's much better than it was before and this occurred after the fourth cycle of treatment and it dips down, but you wouldn't make an assessment based on one lab count. You would watch and see what happens over time because it's normal to have these fluctuations, but what you want to see is over time it gradually goes up instead of down, down, down. Does that make sense? Any questions? Yes? You want to talk into the mic?

Q31: Following the four cycles of the Azacitidine, approximately how long should a patient stay on? I know it's individualized, but... I mean...

Sara M. Tinsley: That's a very good question. Did you all hear that? She said how long do you stay on it once you have a response after the fourth cycle? Does anybody know the answer?

Q32: Until it no longer works.

Sara M. Tinsley: That's right. You continue it for as long as it's working or until a person says they can't take the side effects anymore and I have had someone who was on treatment for over four years and had a beautiful response, but she didn't want to do it anymore. I think she was severely depressed because she kept thinking she was anticipating I'm going to lose my response any month now. I'm going to lose my response and then I'm just going to die and so we had to work with her. I think she didn't come off therapy, but you continue it for as long as it's working and the person is not having side effects that they don't feel are tolerable.

Any other questions? That was a good one. Yes.

Q33: (Inaudible 2:10:44)

Sara M. Tinsley: I couldn't get mine to turn on either. That's actually a very good question that you brought up and I've had... I wanted to just emphasize that that so I've had patients stop the treatment when it was working and then there's no guarantee that it would work again when you start again. So, I've had some patients say well, so and so said that I've had three years of it. I should stop and then if starts back again I can just start the treatment again and I'll get back into remission and that's not necessarily what happens.

Q33: Thank you.

Q34: Is treatment after a transplant or before a transplant?

Sara M. Tinsley: This was before a transplant, I believe, but remember in our low risk disease they might not be going to transplant. Usually if someone... if you're just trying to keep that blast count from going up and you're trying to get them to transplant then you would probably... you would stop this before they go to transplant, but you want to time it with the transplant physician as to when you're going to give your last cycle of therapy and when they're going to go to transplant because you don't want to give a lot of time in between and there's a lot of logistics or planning involved and when the donor's available, when they have time available in transplant and when the patient's ready where they're at in their cycle. That's a good question. Like where is this patient? This is just snapshot of four cycles, but what's happening with the patient really tells you whether you're going to continue giving it or whether they're going to go to transplant or what you're going to do.

And this is a really encouraging slide and I have had patients that been on Lenalidomide for over 10 years and had a sustained response especially with 5Q- type of MDS and this is graph of someone who has been on the Lenalidomide treatment or Revlimid treatment. We also have like two or three names for the same drug just to keep us on our toes. Right? It's like are we talking about the same thing? Yes. This is Revlimid or Lenalidomide and, again, this is graphing a person's blood counts. Again, you have the hemoglobin in pink and you can see when they started their hemoglobin was nine then they went down to it looks like 7 ½, but then over time you can see these are really pretty normal looking hemoglobin levels, 12 and above, and then like I was saying Revlimid works well for the red blood cells, but the other blood counts normally can take a hit. They go down and you want to see them kind of level out at a safe level for a patient and this, the yellow one, is the platelets again and we're going to look at this bar for platelets and they started at over 180,000. So, well within normal, but you see them come down quite a bit too close to 60,000, but then kind of stay between this 80,000 and 100,000. So you just monitor for signs and symptoms of bleeding and look at your medication list what other medicines are they taking that can interfere with platelet function, but really above 50 the person should be okay without any major bleeding episodes and even have surgery for a lot of people up around 100 and sometimes 50 for major surgery... I mean, minor surgery and then the white blood cell count you can see this is low but it's kind of staying within a safe range. I don't know what the neutrophil count is but normally you would want to maintain a neutrophil count greater than 500 to continue taking it. So, are your other counts low? I'm sorry to keep focusing in on your, but...

Q35: No. Actually right now they're all normal.

Sara M. Tinsley: Yours are all normal.

Q35: Low in the normal.

Sara M. Tinsley: Then low and the normal. That's really good. I do have some women that I've been following for over three years that are on a study using Lenalidomide plus or minus Procrit

and they've struggled with their neutrophil count and they don't have 5Q- syndrome. They have just low risk MDS, but we've had to reduce their dose and hold it and monitor them closely for infection and mainly neutrophils is what I've seen with them, but really over three years for both of them without a need for transfusions which was different than before.

So, you really I want to encourage you to become a partner in your MDS journey along with your healthcare team and your support system, your family and your friends. This is where strength comes in numbers when you're fighting something that's scary and new and this is looking at your MDS Manager. So, you want to maximize each treatment option, become, again, in your MDS journey. There's caregiver self-care. Ask for help. You want to stay as healthy as you can be and not just say oh, well, I have this. What does it matter? You still want to take care of yourself and monitor for other potential healthcare problems and you want to build your MDS plan. Look at the *Building Blocks of Hope* and learn to track your own progress in your MDS Manager and this we talked about know what your IPSS score is or your IPSS-Revised. Some of the patients that I take care of will ask me am I stage four? That's really more like a solid tumor type of thing where you have like a breast cancer that then moves to your bones or some other place or the lungs. So, that's the staging system for solid tumors when you have stage one through stage four, but what we have for Myelodysplastic Syndrome is that IPSS and the IPSS-Revised.

Q36: So, there's different treatments that factors go into... the different treatments that are available for MDS. Your things that go into the IPSS-R risk category can change. Does that mean that your risk category changes as you progress during your treatment?

Sara M. Tinsley: Those are really for at the time of diagnosis, but I can tell you I had patients... I've filled in a lot of data like trying to look at low risk and high risk and how long people live and things like that and sometimes even though they start at high risk after they had some therapy they... some of the patients I've seen really are behaving like low risk disease and all of our clinical trials are really, at least at Moffitt, they're structured around whether they had low risk or high risk disease. So, that's a good question. It's not dynamic. It would be nice if we used a dynamic but there's lots of different staging systems for Myelodysplastic Syndrome, but at least if you learn what yours is then you can see when you go to ClinicalTrials.gov you can look for clinical trials close to you that you might be interested in participating in and you could take those to your doctor. I've had patients bring me trials and say what do you think about this one or what do you think about this other one? Any other questions? No.

So, when you go to your hematologist we always check a CBC with differential and we check a chemistry profile. I think if you can learn how to look at your own blood work and track those in your MDS... this *Building Blocks of Hope* there's a transfusion tracker. You can track your transfusions of packed red blood cells, track your platelet transfusions and really get a feel for how your blood is doing. Are you getting better or are you getting worse so that you can have those kind of questions with your hematologist and I usually provide all of my patients with a

copy of their labs. A lot of patients look on the portal and our portal allows them to graph it. So, that's an easy way to look at a lot of lab values easily without comparing one at a time. It'll graph it out for you. There's usually like a box you can click. Do any of you graph your labs? Yes. Some do. Or you just know where yours hang out at? Yeah and I would look in your differential, the differential part of your complete blood cell count tells you what type of cells are there. So, if you are seeing blasts and those are increasing that's a sign that you could be getting into trouble and then you want to look at your neutrophil count and see how many neutrophils you have for your risk of infection and then platelets for your risk of bleeding and then, of course, taking your medications as prescribed, keeping your appointments. Ask about symptoms that need to be reported immediately. For my patients that have a platelet count 10,000 or less if they have any bleeding I want them to call us immediately because sometimes a nose bleed or a mouth bleed is a sign that their platelets have dropped lower than the last time I saw them and then the frequency of your lab draws should match up to how low your blood counts are. If your blood counts have been very stable and they're not changing and they're pretty functional you might not need to be checked that frequently, but if you're needing frequent platelet transfusions or frequent blood transfusions then you may need to be monitored more closely so that you don't get into a crisis type situation and then you want to ask your doctor about the goals when you're getting treated. Is the goal to decrease your transfusions or to prevent you from developing acute myelogenous leukemia or is the goal to get you to transplant? Yes?

Q37: I think watching everything, your appetite, if it's changed, if your fatigue, if you're... there's just a lot of different things that you can watch. A lot of people say look at the bruising and look at the bleeding. In our instance, he never bruised, he wasn't a bleeder. He just... we could always tell by the fatigue or whether or not he could walk to the mailbox or back or just other different symptoms and signs. So, you have to watch all of that not just am I bleeding or am I bruising.

Q38: Because I'm also on a blood thinner. So, I have a mechanical valve. So, my threshold is 50 and below is we have to consider whether or not to get platelets and it's just a balancing act between everything else, but having it for 14 years I've kind of been doing that anyways before the MDS, but as long as you can keep up with your levels you can kind of have an idea and you become an advocate for yourself with your health team and just keeping yourself informed and not being afraid to ask questions whether you want to know the answer or not. It's better to ask and know because then you guys can plan on your next step.

Sara M. Tinsley: Thank you. That was very helpful.

So, not just numbers but also your symptoms. A lot of my patients they get more fatigued when their platelets are low. I don't understand that, but it's something that we see because we think fatigue is more linked to hemoglobin, but patients with Myelodysplastic Syndrome have a lot of fatigue, but if it changes for you then that would be a reason to call your healthcare team, too,

and then financial assistance programs with different... the different therapies. The Leukemia and Lymphoma Society is a great place to start for a lot of these.

And this is getting back to what he was talking about. Shared decision-making helps your healthcare team align our treatments with what you want, what you desire for your journey to look like when you have Myelodysplastic Syndrome. Your preferences, your goals, your value. That's really what defines the best treatment for an individual.

And this is really talking about making the most of ever office visit. What do you want to get out of this visit? You want to write down the top three things you want to discuss and focusing on your agenda will help you make the most of your time and it's a really... we have like these tight deadlines. I have patients scheduled every 15 to 30 minutes. So, it's really hard on both ends to... for us to meet your need and for you to get out of the visit what you need, what you need to learn. So, if you make a list that will help and if you can bring somebody with you that helps, too, because two sets of ears is better than one and if you have any changes in your healthcare since your last visit you want to keep a list both of not just medications that are prescribed but over the count medications that you're starting to take like vitamins, herbs and supplements. Keep track of your symptoms and side effects and then your transfusion records and this is just, again, talking about making the most of your visit.

And then the caregivers, all the caregivers in the room we thank you so much for showing up for this and showing your support. We want the caregivers to stay healthy also. So, don't burn yourself out. Try not to burn yourself out. Get enough sleep and good nutrition and exercise and ask for help and your support team. There's calendars that you can coordinate your calendar so you can be there with each other when it's most needed and then volunteers in your community and this is, again, just coordinating your efforts around appointments and transfusions and transportation, those type of things and continue to enjoy the things that you love and live with your MDS, balancing your lifestyle, your balanced diet and your health habits.

And this is really... a lot of the studies for fatigue management are looking at moving and staying active as being important to combat your fatigue and sometimes when I ask patients to stay more active or to become active they look at me like I'm crazy because it's hard to get up and get moving when you feel bad, but if they're not moving at all we try to set short goals like even if you can get up and walk just to the mailbox every day or walk for five minutes and then try to increase it that this has shown to really help with improving the fatigue. We also have wonderful physical therapists that can go into the home or a lot of times they're at the facility. We have physical therapists at Moffitt, but I've tried to set up physical therapy at home to try to get patients moving. You want to maintain as much function as possible. That will help you tolerate any type of therapy and they can also evaluate you, the physical therapist, for any type of assistive devices like rolling walkers with seats or bedside commodes or things like that that you might need if you're having diminished strength. Our legs and our butt is where we have a lot of muscle and so patients feel weakness in the legs when they have more anemia and so that can be

a real problem even just going from seated to standing can make some patients feel short of breath. So, you might need some help there and eat light before you go to bed and just try and to track your number of hours of sleep. They have these little Fitbit devices and a lot of monitoring devices for physical activity that help you keep track of how much you're sleeping, how much you're drinking, how much you're moving and really if you can focus on the things that you have control over I think you'll find that you can feel better overall like getting enough hydration even just being a little dehydrated can contribute to your fatigue. So, just something to think about and good sleep habits and this is the drinking slide and really if you're only drinking a couple glasses a day it's not enough. You need to increase your fluid intake. If you have a cardiac condition you might want to discuss how much to drink with your cardiologist so that you don't run into problems and get highly nutritious foods into your diet with good calories and protein.

And then what can you do to avoid infections? Monitoring your blood counts. During these active therapies for the first eight weeks and then depending on what you get to on your blood counts these immunizations, a flu shot every year and then pneumonia vaccine and we don't recommend generally the shingles vaccine for immune compromised patients because it's a live vaccine and it could make you sick and then these are things that we go over with the patients who are neutropenic. Avoid people who are obviously ill. That's probably a good idea even if you're not neutropenic just so you don't get sick. Washing your hands often and those hand sanitizers.

Yes?

Q39: Sorry to interrupt.

Sara M. Tinsley: Oh, that's... I want to be interrupted.

Q39: Finally came to a place I want to ask my question or get my information. Even though my hemoglobin levels were increasing I was constantly having respiratory infections, colds, bronchitis, etc. Made you feel bad so like I asked the doctor. He started me on infusions of Gammagard. It boosts your immune system and it's worked well. I haven't had a cold now in two months after starting that. So, is that something that's very common? I don't see it mentioned anywhere. I've taken boosters. They say take it once a month, the next three or four hours an infusion but it's sure worth it if anybody else needs that.

Sara M. Tinsley: He's saying he gets immune globulins. It helps him with infections. There's a way to check to see if you're low on your immune globulin levels if that's contributing to your infection. Some patients who've had lymphomas or other type of treatments with Rituxan or just born with decreased immune globulins that's one of the things, strategies, that we can use if you're having repeated infections is infusions of intravenous immune globulin. It's a pretty expensive treatment and there's specific criteria you have to meet. So, that would be something

that you want to discuss with your physician if you're having repeated infections and you've ever been treated with Rituximab, a monoclonal antibody that can deplete IGG levels. Anything else?

Some doctors use preventive or prophylactic antibiotics when neutrophils are less than 500, but that's one of those individualized depends on your doctor as to whether they do that or not. I work with about eight different doctors and only I think three of them do like if the person's neutropenic, neutrophils less than 500, they get put on a preventative antibiotic but the other ones don't think that that's necessary.

And for bleeding, your risk of bleeding increases when your platelet count falls below 50,000. You want to talk with your healthcare team about recommendations and, again, during the active weeks of treatment with any of the active therapies like Lenalidomide, Azacitidine or Decitabine during those first few months is when your blood counts are going to get the lowest including platelets and you want to be followed closely and you want to avoid the class of drugs that's called nonsteroidal anti-inflammatories or also NSAIDS if your platelets are consistently less than 50,000 unless you have to be on them for other reasons, but that your hematologist has discussed with the cardiologist or they're aware that you're taking either aspirin, ibuprofen, naproxen. All of those are in that class. They can also be... they make your platelets not stick together. So, if your platelets are low and you're on those then that's like two things that can increase your risk of bleeding. Also when you're neutropenic and you take things that can mask an infection or lower your temperature so that it would be more difficult to find out if you have an infection just to be aware and make sure your healthcare team is aware of other medicines you're taking not just your prescription ones, but over the counter and then this is talking about any type of blood thinners. Coumadin, Xarelto, Eliquis, Plavix, you want to discuss those and make sure your healthcare team knows that you're on those if you have a low platelet count especially 50,000 and below.

And just making sure you have the list of everybody's contact information that you see and try to... it's very difficult to coordinate all the different specialists. I can appreciate that, but if we know their name and their contact information then I can reach out to your referring physician or you consultants and discuss how your treatment for MDS may interact with what they have planned for you just so we're all communicating.

And then palliative and supportive care for cancer. This is really the new wave. Palliative care doesn't mean hospice. It's a therapy. It's a form of supportive treatment that goes along with active therapy and the World Health Organization recommends that all patients who have a life threatening illness can benefit from palliative care and their focus is not on curing the disease but really helping patients have a better quality of life and help improve... prevent suffering and it's usually an interdisciplinary team focusing on symptom assessment and not just focusing on the patient but also on their family members. We have a palliative care service at Moffitt and I moonlight with them because I'm trying to learn how to help patients with all of their symptoms.

They also talk about... they have training and discussing goals for end of life care with patients so that when it's... we all have a time when our time is up that things are done for you and for your family that are in line with what you want done. So, just thinking ahead and trying to plan that and then it's palliative and supportive care. Those are kind of interchangeable terms.

And then if you look under your MDS Plan, there are several tools available there to help you track and manage your journey and then there's also a mobile application. If you have an iPhone or Apple system or Android and these are the features that are on there. There's an MDS profile where you can calculate your IPSS-Revised score, look at your bone marrow results and also incorporate your molecular profile and, again, it's really hard to understand all of this all at one time, but it's like you usually get little bits and pieces along the way and one day you'll look back if you're really trying to understand it and you'll realize you understand a lot more than when you first started. Tracking your labs, your transfusions, treatments, your contact information, symptom tracker, medications. You can download reports to print, upload reports and sync your calendar and then there's also live support through the MDS Foundation. I know I've had Audrey contact me with patients who've called in asking questions and I try to answer her in a timely fashion if she needs help asking a question that a patient posed at the MDS Foundation and then there's... there are the MDS Manager key features.

And then hope. "Hope is a thing with feathers that perches in the soul and sings the tune without the words and never stops at all." So, keep at it. There's always hope.

And then MDS patient outreach and advocacy program and Audrey is who I was talking about before that sends me E-mails that you could call and she does reach out to other healthcare providers.

And now anybody have anything they want to share or discuss or have questions about, things that were confusing that... there's no bad question. No.

Q40: I just have some suggestions. Going through what we've gone through I...

Sara M. Tinsley: He had a transplant?

Q40: He had a transplant.

Sara M. Tinsley: How long ago?

Q40: He's 2...

Q41: Two hundred forty-three days post.

Sara M. Tinsley: Two hundred forth-three days post.

Q40: Post-transplant. Yes.

Sara M. Tinsley: But who's counting. Right? So, not quite a year.

Q41: Not quite a year.

Q40: As a caregiver, I think it affects... it affects the caregiver as much as it affects the patient and the caregiver needs to be the one that's positive, the one that's upbeat, the one that's always making sure that whoever you're taking care of is taken care of well. So, always remember as a caregiver to use your resources of your friendship, your fellowship, your... anybody. Your peer groups, your church, talk to the doctors and stuff and always to be there with them because it takes a toll on the caregiver, but you don't want to let it take over you either. You say don't... you're not living with MDS. You're living MDS, but don't let it take over your life and as a caregiver don't let it take over you either.

Sara M. Tinsley: Where did you have your transplant?

Q41: Here (inaudible 2:42:15) is my doctor.

Sara M. Tinsley: Okay. Very cool and who was your donor?

Q41: My twin brother.

Sara M. Tinsley: Your brother. Very good. Anybody else have questions? Yes.

Q42: My question is (inaudible 2:42:29) and he has to have blood transfusion once a week. I didn't (inaudible) get it set up where she can draw the blood and access the port. How long can the port stay accessed or does it have to be changed every week?

Sara M. Tinsley: Different home health agencies and hospitals have different policies. The one I'm familiar with is that the needle has to be changed once a week.

Q42: Once a week.

Sara M. Tinsley: I don't know what the policy is here. Once a week the needle for the port?

Q43: (inaudible 2:43:10)

Sara M. Tinsley: I really...

Q42: And is that because of the risk of infection?

Sara M. Tinsley: I believe so. Yeah.

Q42: The white count is low and the neutrophil count is low. She wasn't sure what the rule was going to be and so she had asked me to ask the question today to make sure. I don't think the oncologist is going to allow her to leave it accessed. I think that she's going to tell her no because she was worried about even having a port in the first place.

Sara M. Tinsley: Because of the risk of infection or bleeding? Infection. Yeah. A lot of places are using those peripherally inserted central catheters, but those the similar risk, but they can be taken out easy. You just pull them to take them out but they have to have dressing changes every week and flushed every week and for the PICCs they have to wrap them and not get them wet when they take showers. For ports, too, if they're accessed you can't really get them wet when they're accessed because that will be a risk for infection.

Q42: Thank you.

Sara M. Tinsley: You're welcome. I wish for a little while I moonlighted with hospice and I took care of a patient who had MDS that progressed to acute myelogenous leukemia and we tried to give him transfusions in the home, but that's not something that's commonly practiced. Even hospice allowing transfusions or transfusion in the home, but I know in the UK that's one of the ways they're trying to help people not have to spend a lot of their time at a healthcare facility at an infusion center is the nurse comes to them and transfuses them. That would be... that's a little scary like that one transfusion I did as a nurse in the home we had problems getting the blood to drip in and that's like nerve-wracking, but I think anything we can do to help minimize the check in, the wait times, a lot of those little processes really take away from people's quality of life that they're frustrated all day long trying to get a hold of the doctor or trying to get in for a blood transfusion. That's valuable time. So, that's one of the things I do with my patients who are needing regular transfusions is making sure they have a schedule and that I'm checking them and that they have a place reserved to get their blood transfusion when I think they're going to be in the unit. So, things like that trying to help guide like I normally drop my hemoglobin at this time period, can you check my blood then? Like being proactive like that I think helps. Sometimes it's unpredictable though.

Any other questions? No. I wish you all the best and thank you so much for paying attention and coming in. You have a question?

Q44: How many patients we have in here.

Sara M. Tinsley: He wants to know how many patients. So, nine patients and a lot of caregivers.

Q45: (inaudible 2:46:45)

Sara M. Tinsley: How long have you been diagnosed? Do people... 2011 November and you're needing regular blood transfusions?

Q45: Never had one.

Sara M. Tinsley: Never had one. Very good. So, Aranesp is doing that for you. How much do you get?

Q45: (inaudible 2:47:06)

Sara M. Tinsley: Every couple weeks or every three weeks. Every three weeks. Very good. So, yours sounds like it's low risk disease and then you had the...

Q46: October last year.

Sara M. Tinsley: October last year.

Q46: (inaudible 2:47:18) blood types.

Sara M. Tinsley: Yeah. You're changing to your donor's blood type.

Q46: He said he didn't know from before the transplant, but if your donor has a different blood type than you you will use their blood type. So, sometimes there may be a period when you need transfusions through the gap. That's why (inaudible 2:47:48) and I get O- and my brother's A and eventually I will go to A, but my brother and I didn't always agree as kids (inaudible 2:48:01).

(Laughing)

Sara M. Tinsley: How long did Revlimid work? Are you still on it?

Q47: No, I didn't want to be.

Sara M. Tinsley: Side effects?

Q47: Side effects, so I stopped it but the effect is still there. The hemoglobin count which had been averaging seven with the transfusion a month is now up to... it's gone down a little bit. In the past three months. (Inaudible 2:48:28)

Sara M. Tinsley: Very good. That's a pretty nice hemoglobin. Anybody else? Yes?

Q48: (inaudible 2:48:35)

Sara M. Tinsley: Normally, you don't stop it if it's working. Now, if you were having like specific problems that they were trying to see if they held it if your blood count...

Q49: (inaudible 2:48:57)

Sara M. Tinsley: I don't know then. I don't know what they were thinking and you had another question?

Q50: (inaudible 2:49:07) I'm kind about my MDS in May of 2011 and the doctor said I would have leukemia in three to four months and I'm a high risk and he wanted me to take chemo the next day five days a week for six months and I couldn't believe it. So, I made a trip to Emory and talked with Dr. Heffner. I'm not a high risk. I'm not ready for any treatments for 6 ½ years I took anything. I'm still kicking and doing good.

Sara M. Tinsley: Yes. Very good.

(Applause)

Q50: (inaudible 2:49:46)

Sara M. Tinsley: So, I do help out with doing the new patient consultants with the physicians in the MDS group and I would tag onto that if you haven't been to one of the designated centers MDS Centers of Excellence and an MDS expert you really... that kind of sets it as to what your risk assessment is and you know that if you're at an academic center and a Center of Excellence for MDS the hematopathologist are specially trained, you're going to get the cutting edge, the best treatment and the best advice for your MDS, I think. Yes?

Q51: (inaudible 2:50:29) six years, but I already been on chemo one year.

Sara M. Tinsley: Which kind are you on?

Q51: It was the...

Sara M. Tinsley: Azacitidine?

Q51: That was one of them. I can sometimes (inaudible 2:50:47) with that and...

Sara M. Tinsley: And you've been on it a year?

Q51: Procrit (inaudible 2:50:52)



Sara M. Tinsley: With it.

Q51: (inaudible 2:50:55)

Sara M. Tinsley: Okay. Very good. You look beautiful. Yes? Anything else? Alright. Well, thank you very much for spending the Saturday with us.

(Applause)