Speakers
Selina Luger, MD
Emmanuel C. Besa, MD
Sandy Kurtin, RN, MS, AOCN, ANP-C

Sandy Kurtin: Good morning, everyone. Welcome to the MDS Foundation Patient Forum. My name is Sandy Kurtin. I am a nurse practitioner in Tucson, Arizona and I thought I'd just come out here and enjoy a little humidity because it's very… I think our humidity is about six percent and you can tell from my hair that you have way more than that here. It's my pleasure to have you all here. I am sorry about our tight quarters. We're used to having a much larger room, but we're all going to get to know each other very well today anyway. So, we thought it would be a good start just to put you all close together. We have some presentations for you today, but mostly we want this to be very interactive, an open discussion, answer your questions. We have Dr. Besa here. We have Dr. Luger who we're trying to locate. She's probably tied up in clinic. She works here in the Cancer Center which is why we ended up here in this room and you have resources on your table. This is a new project, a work of passion, a big part of my life called the *Building Blocks of Hope* and we're going to go through this in a little bit more detail later on this morning and so each family should have… take one of these to have. I'll be showing you some of the digital capabilities of this a little bit later in our agenda. There is a bathroom. They want us to use the one that's… if you go straight down the hall and through the door, there's one just to the left. They prefer that we have you use that as patients because there's an emergency cord in case you need that and luckily we're amongst many medical professionals here. So, we're in good hands. Hopefully, none of us need that, right? And then please if you have questions, jot them down so that we can come back to them later on, raise your hand, interrupt us if need be and we are looking forward to a good meeting. We have a lunch break that will be at noon and we're going to try to mosey on out onto the patio here so that we have a little more space and some fresh air. So, we'll hopefully get them to set the food up here and then you all have an opportunity to sit and chat at the tables together and then we'll reconvene and then this afternoon, it really just have open discussion and try to answer whatever questions you have. So with that since Dr. Luger is not here, I think maybe we can start by just doing a quick round of introductions. Tell us who you are and why you're here and then we'll go from there.

Mary Weisenborn: My name is Mary and I'm here with Pat. She's the one that has MDS. I'm curious.

Sandy Kurtin: Curiosity is a good thing.

Pat Thompson: My name's Pat. I had it for like 2 ½ and I don't have any kind of treatment or nothing yet. I just take B12 vitamins.

Elizabeth Biggs: I'm Elizabeth, Betty Biggs, and we're from Greenwood, Delaware and came up here for this to find out, get some information and I'm like Pat, I have only had it for a couple of years now and I'm not on any medication or anything.

Jay Biggs: And I'm her husband Jay and I tag along. Where she goes…

Sandy Kurtin: That's what husbands are supposed to do.

Paul Rothstein: I'm Paul and I've had a problem for about eight years. My white blood cells are dropping and my platelets. So far, no treatment and we're waiting for the other shoe to drop.

Eileen Rothstein: I'm Eileen. I'm his wife and part of his support group.

Sandy Kurtin: Wonderful.

Linda Zurcher: I'm Linda. My sister-in-law, Doris, has MDS diagnosed around February/March. She's getting transfusions every two weeks, having a hard time, so I'm here just to learn a lot more about it.

Doris Zurcher: And I'm Doris and I have MDS since I was originally starting to have problems in December of this past year and diagnosed in February and, again, I've been having transfusions every two weeks and I've been on some other medications, Procrit. I get shots every week and I get… I have taken Revlimid for two and a half months and it didn't do anything for me. So, that's not a option anymore. So, I'm trying to find out more information and what options I have.

Sandy Kurtin: Okay. Well, hopefully (inaudible 5:09) that can answer some of those questions.

Donna Zurcher: I'm Donna. I'm Doris' sister and I've been helping her through this.

Joyce Mueller: My name's Joyce. I've been diagnosed the past year and I am getting transfuse… In fact today, I'll get my second transfusion. Dr. Luger is my doctor and I'm in a clinical trial now with Revlimid which I started a couple weeks ago and took it for three days and broke out in hives all over. So, off of that right now. We'll see what the next step is.

Bill Mueller: I'm Bill. I'm her husband and, again, part of her support group and here to find out what I can do to help.

Tara Lanzalotti: I'm Tara and this is my mom.

Suzanne Campbell: I'm Suzanne. I'm a retired oncology nurse, worked a lot with breast cancer patients who a couple of them had to have chemo and went into MDS as a result of the chemo and I'm here with Jim.

Jim Wetherill: I'm Jim. My wife had MDS and I've be just interested in following the development of the treatment for it.

Ray Malles: I'm Ray Malles, Warminster, Pennsylvania. I was diagnosed in November of '05 and I'm 83, so I'm still plugging along. If I could instill anything into your minds of those attending here, I've attended all together I would say with MDS and aplastic anemia forums that

are put on about 10 around the country and every chance I get that there's one close by I go and I have learned something from every one of them.

Ellen Steely: I'm Ellen. It's my first forum. I'm diagnosed a little over a year ago and I just started Revlimid about a month and a half ago. I know a little bit about it because, ironically, my son-in-law who's 52 was diagnosed about 6 years ago.

Phil Miller: I'm Phil Miller. After a bout with colon cancer about 11 years ago, they… the doctor wanted did a little drilling into my bone marrow, disappointed he didn't find oil, but he did find the Myelodysplasia and it's been the same, at the same level, as it was 11 years ago today except my blood count keeps going down. So, that's my problem. It's the deteriorating blood count.

Joan Miller: I'm Joan. I'm his wife and I'm here to get a better understanding of living with MDS and Bill takes the B12 (inaudible 8:12) with some injection they've offered to give him, but he hasn't started any (inaudible 8:18) get his blood pressure (inaudible 8:20).

Bob Wolfe: I'm Bob Wolfe. I was diagnosed with MDS RARS eight and a half years ago. It's a low risk category of MDS and it's only red blood cell (inaudible 8:42) and it was about a year or two in observation, but since then it progressed through pretty much all approved treatments, medical science, Revlimid, (inaudible 9:01) because (inaudible 9:07) clinical trials (inaudible 9:10) label passed right now (inaudible 9:14) and I'm (inaudible 9:20) independent. I've gotten to the point where I was having transfusions every three weeks, but the experimental drugs appear to be pushing that out a little bit.

Barbara Wolfe: I'm Barbara. I'm his wife. I run up and down the stairs a lot because of the low red blood count, get out of breath, so I go (inaudible 9:40).

George Mako: I'm George Mako. We're from New Jersey and I have MDS with a low platelet count and the puzzling thing is I'm being treated here, by the way, with a Dr. Hexner (sp? 10:00) who's excellent and also there's a doctor in Jacksonville, Florida at the Mayo Clinic, but the puzzling thing for me is I've got arthritis and that's painful. So, I know I have arthritis. With the MDS, I feel no anything. So, you kind of like put it off in the back. Maybe about 18 years ago, I was treated for cancer with radiation treatments. From that point on, the blood platelets consistently went down from normal to where I'm plateauing now for about the past 2 years and that number is in the 20,000s which is, I guess, pretty low. So, we're in a wait and see mode and I don't think anyone (inaudible 11:01) this (inaudible 11:03).

Gloria Mako: I'm Gloria Mako, his wife. He's diagnosed with the MDS now about 10 years ago and I'm his researcher. George does not like to turn the computer on. So, I'm the researcher and I'm the reach out and the E-mails and talk to all kinds of people around the country for information.

Scott Sample: I'm Scott and I diagnosed with MDS last March. Part of that when I had a biopsy that day they gave me two transfusions, but ever since then I haven't had the blood transfusions, but if my red blood count goes down every week below 10, I go in for a shot and I have a problem with my white count, too.

Jane Sample: I'm his wife Jane (inaudible 12:00).

Valerie Shane: I'm Valerie and I'm here with Scott.

Scott Megaffin: And I'm Scott. I work for a small pharmaceutical company over in New Jersey and we have a new drug that's in development for MDS. We work closely with the MDS Foundation and we're optimistic that in the future it'll become a new alternative for the treatment.

Steve: I'm Steve. I'm with Novartis and I'm happy to see any developments come along including yours because it's so important. I mean, it's so meaningful to see patients (inaudible 12:38) survivors as well. It makes me feel more meaningful about my job and my life.

Sandy Kurtin: Good.

Brenda Hawkes: I'm Brenda Hawkes. I'm with the Diplomat Specialty Pharmacy and if you're taking Revlimid and/or XJ, you may get those prescriptions filled through a specialty pharmacy like us and I'm here just to support you and to learn more about what you're gong through and what we can do better (inaudible 13:00).

Sandy Kurtin: Lovely. Alright. Well, wonderful. I'm (inaudible 13:04). And I'm Sandy Kurtin. Nice to meet you and I'll let you get started. Okay?

Selina Luger: Good morning. I'm Selina Luger. I am a physician who treats MDS and leukemia here at the University of Pennsylvania. I'm going basically give you a general overview of kind of what MDS is and it's going to kind of the ways we think about it and some of the treatments available and then Dr. Besa and I will kind of open up the forum for some questions.

So, MDS or Myelodisplastic Syndrome, as you know. I thought that the best way to kind of start is to kind of explain to you what a normal bone marrow is and then we'll talk a little bit about what MDS is. So a normal bone marrow is if you think of a chicken bone, kind of you break it open and you kind of see the stuff that's in the middle of it. That's your actual bone marrow and that's where your normal blood cells are being made and it's supposed to make a whole bunch of different types of cells. It starts off with a very early cell and then kind of branches off and decides what kind of cell it wants to become. Decides if it wants to become what we call a white cell, a red blood cell or a platelet cell and each of those have different functions. So when you look in your blood, you're supposed to see a bunch of different cells. See there a bunch of cells we call red cells. There are other little cells that we call platelets and then there are these larger cells that we call white blood cells. Red blood cells carry oxygen. They carry their oxygen on a molecule called hemoglobin and a normal hemoglobin should be somewhere between 12 and 16 and you'll all be familiar with some of these numbers because you monitor them with your MDS. Without enough red cells, you don't have enough oxygen because you don't have enough hemoglobin and so you feel weak and you feel tired. White blood cells. White blood cells are important to the immune system. We have a whole bunch of different types of white blood cells. Some of them care called lymphocytes, some are called granulocytes and neutrophils. Some are

called monocytes. Typically, the number you'll hear about in normal white blood cell count is somewhere between 4,000 and 10,000 and without healthy functioning white cells, we can't really fight infections very well and platelets, these are these little cells that I found in the blood. Those are the cells that help the blood clot properly. If you don't have enough platelets, you don't clot properly. Normally, you have somewhere between 140,000 and 450,000 platelets. We usually don't use the thousands when we talk about them. When we talk to patients, we'll say your platelets are 9 or your platelets are 100 or your platelets are 200. You don't use the… We're talking about… Well, here we're talking (inaudible 15:31) say in the thousands. You need over 100,000 really to be normal. If you're going for major surgery, you probably need somewhere over 50,000 and once you get below 20,000, you're likely to bruise really, really easily and if you're below 10,000 you might bleed for no good reason even if you don't bump yourself. So normally, your bone marrow has in the center you make the cells. Those cells decide what they want to become. That's what's supposed to happen and just for example, these are white blood cells. They go through various types of maturation. They're very early cells. They're kind of the machinery is the largest part of the cell, kind of the part that determines how the cells are dividing and as they go through I'm going to kind of say childhood, adolescence and adulthood, only the adult cells are supposed to come out into the blood. All of these are supposed to stay in the bone marrow while they're maturing and then the adult ones are supposed to come into the blood and perform the functions of what they're supposed to be doing.

So Myelodisplastic Syndrome, the definition is myelo is just bone marrow and dysplasia is just funny looking. So a Myelodisplastic Syndrome really just means you have a bone marrow with funny looking cells and what happens is you make too many cells that really can't do anything useful. That's what happens when someone has Myelodysplasia. It was actually first described back in around 1913, but it really didn't get a category until around the 1970s, a one that we recognized as an entity. So until then there were only like a dozen cases in the literature because no one really knew that all of these things are really the same thing and originally it used to be called pre-leukemia because that's all really people understood it was. They saw people who had leukemia and then they saw people who had this beforehand, but in the last several decades we know that this is a disease that very often never has anything to do with leukemia. So, we don't really call it that anymore.

So, we know that the bone marrow is making too many nonfunctional cells and we actually think there are probably about 50,000 to 60,000 cases per year in the United States now given the way we now define it. It's predominately a disease of people over age 60. Seventy percent of people who get it are over age 50 and it's more common in men than it is in women. Now again, people present typically with symptoms related to the low blood count, so if someone is anemic and the majority of patients with MDS will present with anemia. They'll come in short of breath or tired or not infrequently they'll see their family doctor. They'll have chest pain. They'll go have a catheterization done and they'll say, oh, before the catheterization they'll get blood counts and find out they're anemic or they'll send them to have an endoscopy done because they find out they're anemic and that has nothing wrong in endoscopy and they come to see a hematologist because they're not bleeding and that doesn't explain the anemia. So, they try and find out if it's a bone marrow problem explaining the anemia instead. They have low platelet. People might come in complaining of gum bleeding or just bruising in places that they didn't hit themselves or

if they have low white counts they might come in complaining of infections that just aren't going away.

Now, what's supposed to happen is in a normal bone marrow, cells do grow and they die and they're supposed to replace themselves with healthy cells. What happens with Myelodisplastic Syndrome is that these abnormal cells just replace themselves and they don't allow normal cells to be made. We don't know why this happens. In a small proportion of patients, we can identify a prior injury. So if someone has had prior chemotherapy or prior radiation therapy for another cancer, sometimes that actually has caused damage to the stem cell, so they're not able to behave properly, but the majority of patients who have MDS were not able to identify some that that caused it.

Now how do we make the diagnosis? Sometimes we can look in the blood. So, I told you before that only those mature cells are supposed to come out into the blood. We start seeing immature cells or cells that aren't formed properly in the blood then we can sometimes make the diagnosis just by looking in the blood, but more commonly what we see in the blood is what we don't see. We just don't see enough cells and if we don't see enough cells, we have to look back in the manufacturing part to see why we're not seeing them and so we look in the bone marrow and by looking in the bone marrow, we can try and get a sense of what's going on.

So, why do we do bone marrow tests? We do them to make a diagnosis. We do them to figure out a type to give it a label. We also do it to see if someone has leukemia and not MDS. We also do it to try and figure out kind of how we're going to figure out what's going to happen next or get a sense of the prognosis of the disease.

So, what are the tests that we do in the bone marrow? Many of you have these bone marrows, but this is kind of picture of what we're doing when we're doing the bone marrow tests. In an adult… In kids there's bone marrow in all of the bones, but in an adult, there's really only active bone marrow in certain bones. There's bone marrow in your long bones. So, in the bone here and there's bone marrow in your pelvis. So, those are the really good places to get samples to be able to look and see what's going on in the bone marrow.

?: Dr. Luger, excuse me for interrupting, but if you could stand on that side, those of us sitting here could see the screen.

Selina Luger: Sure.

?: Thank you very much. It's very interesting and we couldn't see (inaudible 20:40).

Selina Luger: So, the bone marrow… So, we take a look. We don't… When we don't have to, we prefer not to go into the bone marrow here although sometimes when we will do bone marrow tests in the middle of the chest just when we have trouble getting to the pelvis because of body (inaudible 20:55) or, again, if someone's had radiation to their pelvis and we can't get to the bone marrow. So, there are two different tests that we do. We use a biopsy needle and we use an aspirate needle. We puncture the skin to go into the bone itself to get a sample of the bone marrow. We do something called a bone marrow aspirate where we take out a little bit of the

liquid from the bone marrow and that's really good to give us a good sense to look at the individual cells that are found in the bone marrow. You can see up on top there's a whole bunch of different types of cells that we see in the bone marrow and then we do something called a bone marrow biopsy where we get actually a little bit of the bone and it actually gives us a sense of the architecture of the bone marrow and depending on your age that should look different. So for example, a 20 year old should have 80 percent cells and 20 percent fat while an 80 year old should have 80 percent fat and 20 percent cells. So, not everybody should have the same appearance of a bone marrow and that we kind of get a sense… Also, some people will have a lot of what we call fibrosis. So, there'll just be a lot of scaring in the bone marrow itself. We can't see that when we're looking at the cells and so we need both of those tests to really give us a good picture of what's happening in the bone marrow. So, we look at marthology (sp? 22:05). That's where we actually look at the cells themselves under the microscope. We also look at the DNA or the chromosomes in the cell. That we call cytogenetics and those are probably the 2 most important things that we look at when we're looking at the actual cells in the bone marrow aspirate.

This is what we call cytogenetics or chromosomes. So everybody should have 22 pairs of chromosomes in every single cell in their body plus either 2 X chromosomes if they're a female or an X and Y chromosome if they're a male and we look at those, again, to look at the DNA within the abnormal cells in the bone marrow and that gives us information. So, this is someone with normal chromosomes. So, you can see they have 22 pairs and then they have an X and Y chromosome. So, that's a male. This is somebody who has a bunch of abnormalities in their chromosomes. So if you look up over here, chromosome 8, one of them is the normal length, but one of them is short. If you at chromosome 5, chromosome 8 you'll see they have an extra third chromosome 8. They're missing one of their chromosome 17s and they've got a short chromosome 20 and you can actually… people know, I'm not one of them to tell a prior chromosome 7 from a chromosome 8 by where the little close pin is and the little black and white parts are and they have the ability to… really, they make this whole map for us and give us that information. And as we know is patients with MDS, at least 50 percent were able to find an abnormality in the chromosomes. The most common abnormality involves chromosome 5. You can see you have chromosome 8 abnormalities, 7 abnormalities and about 20 percent of patients will have multiple abnormalities.

So the real question that people have when they show up in a doctor's office with MDS and they have an abnormal blood count of some sort is okay, is it going to stay this way or what do I expect in the future and that's what we really focus a lot on trying to figure out is telling patients kind of what's happening next. Where are we now? What can we do to fix this? And what can we expect in the future? What direction can the disease go? So as I said, most patients will present with a low blood count of some sort and with time the disease can typically go in 1 of 2 directions. With time, the disease will remain stable at some point and that some point the blood counts are likely to get worse and likely to get worse can mean that if they have anemia and need transfusions those transfusions might become more frequent or it can mean that if they have a low white blood count at presentation, they may also develop anemia or they may also develop low platelets. It can also… The other direction that things can go is they might start off with a very low number of immature cells or what we call blasts and with time that number of immature cells can increase and if it increases a lot and if it goes above 20 percent of the bone marrow, we

actually call that acute leukemia and so either one of those things can happen in the natural history of MDS. The time course of that happening is very, very different for each person and whether or not that is going to happen or which direction it's going to happen is very different for each person.

So, each person wants to know what is my MDS going to do? How long will it be before I develop any complications or any possible life threatening complications and what can I do to kind of slow this process down? So, people have tried to answer those questions and one of the most useful things that's happened in the last decade or so has been a scoring system. So, they looked at 800 patients who had untreated MDS and they tried to figure out what can we tell from the time that we look at the bone marrow the day we diagnose it that'll give us a sense of what to tell patients and what they figured out is if you look at 4 different factors, we get a lot of information. If you look at the age of the patient, you look at their chromosomes, you look at how many of their blood counts are low and you look at what percentage of the bone marrow cells are blasts, we can get information about their risks. We call this the IPSS Risk Stratification and we get a different score based on the number of blasts, the chromosomes and the cytogenetics and that score will then give us an ability to predict what the risk is. If they're a low risk, a low intermediate risk, a high intermediate risk or a high risk and those risk groups are risk groups both for developing life threatening complications from the disease and also risks of developing progression of the disease itself, how likely it is to remain stable for some period of time. So somebody who has an anemia, no matter how severe that anemia is, they'll definitely have cytogenetics and doesn't have a high number of blasts in the very low group and is likely to stay with low risk disease for years to come, but somebody who has a lot of abnormalities in their chromosomes and also has all 3 of the blood counts low, we get more worried about and we're going to want to do something to slow the process down.

So, our goals of therapy, again, depend on what we think is going to happen with the disease and also the patient. Obviously, one of our goals when possible is to improve the survival, but we also want to control the symptoms, we want to improve the blood counts, we want to decrease the risk of developing leukemia and we want to improve the quality of life of the patient. We have treatments that really are aimed at doing all of those things. So, we have a bunch of different treatment options and there so go from very aggressive such as a transplant to just supportive care alone to a variety of things that we do in between.

So supportive care, again, depends on what the patient's problems are. As I said, the majority of patients will have anemia. So, you want to make sure there's no other reason for the anemia when someone's anemic. Very often we use agent that some of you have talked about, a erythropoietin agent. So your body makes a hormone called erythropoietin normally. When you have a low hemoglobin, it should know to make more erythropoietin, but not all the signals not always there to make as much as it needs to make. So we sometimes measure erythropoietin levels in the blood and if not… body's not making enough to make up for the fact that your hemoglobin or your red blood count is low, extra erythropoietin can sometimes help it make those extra red blood cells. The other problem is we'll give transfusions if that is not the case. Some people get so many transfusions that they end up with too much iron in their blood and so sometimes we give medicine to decrease the iron in the blood from the transfusions (inaudible 28:42), a medicine called XJ was mentioned earlier. That's a medicine we typically use to drop

the iron if we think it's going to cause trouble. People who have low platelets, there are some medicines we'll try for low platelets. If those, again, will get platelet transfusions. We try not to give too many platelet transfusions because the more platelet transfusions you get the less likely you are to have your platelets rise when you get them and platelet transfusion only lasts a matter of days when you do get them. So sometimes people will say why am I not getting them all the time and there's a judgment in terms of when is the right time and when is not the right time to get platelets again in each patient and sometimes we'll give medicines that thicken the blood that if people have low platelets and we're worried about bleeding just because it'll allow us to do something rather than just give platelets if we're running into bleeding problems. Or people have low white blood counts, there are medicines that raise the white blood count, but at least here we typically don't use those unless there are problems with infections.

Then we go onto treating the disease, ways to treat it. There is a small group of patients in whom using medicine to turn off the immune system will actually lead to some improvement in their MDS. We try that in certain situations. There's a group of medications called cytokine inhibitors. So, the thinking is that the MDS is caused by signals, chemicals that are signaling within your bone marrow basically not giving the right signals to the cells to mature properly. There are two drugs in that class. One of them is a drug called Thalidomide that many of you may know that was used in pregnancies many, many years ago. For the same reason that it worked there because it actually turned the signals off in cells, it actually was found to work very well in some blood cancers. Unfortunately, it has a lot of side effects of the doses that are needed to treat MDS effectively, but about a decade ago, there is a similar medicine. So, Thalidomide hasn't been… There's another medicine called Lenalidomide which is also known as Revlimid which is related to Thalidomide which has been shown to be very helpful in MDS in certain types of patients. It is very potent and doesn't have nearly as many side effects as Thalidomide and initially was used in patients who have low risk MDS, primarily patients with only anemia and what they found is that in the first group of about 25 patients, 10 or 11 of them had a tremendous response like almost resolution of their anemia, but interestingly enough when they looked at those patients who have this low risk disease and the improvement of their anemia, they found that almost all of the patients who had the initial response had an abnormality in chromosome 5 and so… and I talked to you a little bit about cytogenetics. So, this is a pair of chromosome 5. So, this is the normal chromosome 5. Every chromosome has a long arm and a short arm. You can kind of see here a little bit of indentation. So, this is the short arm of chromosome 5. This is the long arm of chromosome 5. This one is missing a piece of the long arm of chromosome 5. We call Q is the long arm. It's called the long arm because we have P is the short arm and P is petit (sp? 31:55) in French and they needed something to call the long arm, so they used P for short and they just used Q for long. So, the P is the short arm, the Q is the long arm. So, these people have a missing part of the long arm. So, 5Q-. This is another way of looking for it. So, this is where you're looking at the chromosome. This is something we call fish. This is where you say you're looking at the 2 5s and so the green is the 2 short 5s and the reds are supposed to be the 2 long 5s and so you can see this person is missing the part of the long 5 that they get the right dye for. So, you have both shorts, but you're missing 1 long. So, that's another test that you do to look for that long arm of chromosome 5. These people seem to have had a really tremendous response to Lenalidomide and so just to kind of go through, we have a whole bunch of different types of MDS. Some of them have chromosome abnormalities. I mentioned earlier the most common chromosome abnormality is an abnormality of chromosome 5 and a even small proportion of

those people who have abnormalities of chromosome 5 will have something that we call 5Q- syndrome which is an abnormality of chromosome 5 which only has anemia.

So, this study that was done looked at patients with Lenalidomide. They gave Lenalidomide to patients with low risk MDS. They actually had a study that looked not only at patients with abnormalities of chromosome 5, but they also looked at patients who have abnormalities… low risk disease without chromosome 5 abnormalities, but I'm going focus on the ones with the chromosome 5 abnormality. If you took a look, they did… they took patients who had chromosome 5 abnormality. They had almost 150 patients on the study and 67 percent of them lost their need for any type of transfusion. So, two-thirds lost the need for any type of transfusion and another almost 10 percent lost need for 50 percent of them. The immediate increase in hemoglobin was 5 grams. So, people were starting off with a hemoglobin of about 7. They went up to about 11 or 12. So, it was a significant improvement in hemoglobin. It lasted… When they looked at the 2 year point, most people still had that response. So, it's very, very effective in improving the hemoglobin in patients who have abnormalities in chromosome 5 who have MDS. It doesn't fix the MDS. It doesn't make the bone marrow better. It doesn't prevent the disease from going any further, but it fixes the anemia for as long as it works. It also works… So, it provided transfusion independence in a good number of these patients. It was much better in patients with a 5Q abnormality. Most commonly, these patients get low blood counts while they're getting the treatment, but usually with interrupting the treatment and reducing the dose, you can fix that and there was also… there were also some responses in patients who don't have abnormalities in 5Q.They're not as dramatic and it doesn't happen in as many patients, but it still is something that's worth trying in patients with low risk disease if they don't have significant side effects. The other class of agents that's been approved for use in MDS are agents that we call epigenetic agents. So, what we know is that you have genes in your cells that tell them how to mature properly. You're supposed to have ways of turning those genes on and off. Normally, some are on and some are off in MDS, some of it are supposed to be on or off. So, there are some genes that are supposed to your cells how to mature properly and are supposed to turn off things that are supposed to turn it on that get turned off inappropriately and there have been some drugs that have been shown to turn back on genes that have been turned off when they shouldn't be. One of those classes of genes are called hypomethylating agents and the 2 that we hear about the most are Azacitidine or Vidaza and Decitabine or Dacogen and what we've shown is that both of those agents have been shown to have responses in all risk groups. They decrease transfusion needs and they improve quality of life. They do, however, have side effects and so we typically don't use them until the quality of life of the disease is causing more… the disease is causing more problems in quality of life than the treatment would cause. You have to come into a doctor's office 5 to 7 days in a row. You need to get blood counts twice a week. You often need transfusions as a result of side effects of these medicines. So, we typically use it 1 of 2 situations. If somebody has transfusion needs that are excessive on the basis of the disease that are disease… the quality of life is impacted by the disease itself we think about it or if somebody has MDS that's gotten to that higher risk level. We know that this will decrease the risk level of the disease itself and so we consider using it in that situation. So, this was the original study that was done. It took patients with all different types of MDS and it randomized them. So, half the patients got the treatment. Half the patients did not. Those who did not, if they did not get better which most of them did not, they were then allowed to be given the study drug and then they looked at responses of patients who were on study. The primary end point of this study was a

quality of life study and this is the patients who originally started off not getting treatment. So, these were the supportive care and as you can see over time, their physical function got worse, their fatigue increased, their shortness of breath increased then they started the treatment and when they started the treatment their function improved, their fatigue decreased, their shortness of breath decreased. So even they were getting treatment that may have had side effects, their quality of life actually improved while they were on the therapy. A subsequent study took patients only with higher risk disease, compare treatments to other options either supportive care (inaudible 37:37) of chemotherapy and actually showed that those who got the treatment did better. They had more responses, more complete responses, more partial responses and they had improved survival. So, the group who got the treatment actually had an improved survival rate compared to those who did not get Azacitidine therapy.

The most aggressive therapy that we have for MDS is a transplant and the reason we think about that is that despite the fact that we have treatments available that improve quality of life, that decrease disease, that would decrease blasts, that decrease transfusion needs, none of those have been shown to cure the disease. The only thing that has been shown to cure the disease is a bone marrow transplant, but bone marrow transplants, typical bone marrow transplants, uses high doses of chemotherapy and/or radiation to kill the patient's own bone marrow and has risks associated with it. So, you have to make a decision about if and when it's appropriate to consider that. In a typical bone marrow transplant, what you do is you take a patient, they have their regular blood, they have their MDS blood. You give them very high doses of chemotherapy and radiation. It kills off all of the cells in their system. You give them cells from somebody else, replaces that they end up with healthy cells or that's the way they'll stay for rest of their life (inaudible 38:56) cells, but it's risky and some… the patients who are most likely to do well with transplants are also the patients who are likely to do well with other transplant and live years with their disease without problems. So, you have to make a decision about when is the appropriate time to do it. What this table tries to show you is that those patients who have low risk disease live longer without a transplant than they do with one. Those who have high risk disease, the sooner you do the transplant, the better because they're just gong to run into transplant from the high risk disease.

We do have another option these days that we think of which is something that we call a reduced intensity transplant which makes it less toxic. In this situation, you take the patient who had their MDS. You give them chemotherapy that doesn't kill their bone marrow. It just allows their body… it decreases the number of cells, but lets them accept somebody else's cells. You give them someone else's cells. That person cells come in and lives together with their own cells and eventually over time will take over their bone marrow. So in the ideal situation, you end up where you do the other way in a little bit of a gentler fashion. It still has a lot of side effects associated with it. So, it's still not something we jump to, but it gives us a transplant option in patients in whom we might have not been able to offer a transplant in the past. So, it uses the donor immune system rather than the chemotherapy to get rid of the MDS cells and at Angel, we call it graph versus tumor effect and we've seen some nice responses with it.

Primarily, we get answers to what we should do and how we should do this through clinical trials. That's how we really figure out that we've gotten to where we are today in terms of MDS. We're looking at different schedules of Azacitidine and Decitabine and we're combining those

drugs with other drugs. We're using Lenalidomide or Revlimid together with Azacitidine and Decitabine in higher risk disease. We're looking at new treatments, new ways to do transplant, new types of agents and new ways to kind of deal with platelets.

So overall, MDS is a group of diseases that's characterized by low blood counts and a bone marrow that just doesn't work properly. The bone marrow studies give us information that's important both for diagnosis and prognosis and allows us to follow the disease. The treatment needs really have to be tailored to the patient. Fortunately, we have a lot of new treatments on the horizon and clinical trials are really essential for us to really make progress in this disease and I'll stop there.

Sandy Kurtin: Thanks to Dr. Luger. Does anybody have questions for Dr. Luger and Dr. Besa is going to also then take it from there and field some questions.