Speakers:
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Dr. Stuart Goldberg: Hello. I am Stuart Goldberg. I'm the Director of the MDS Foundation at Center of Excellence in Hackensack, New Jersey, which is right across from New York City and I'm scheduled to give a talk with slides in a little bit about iron overload and transfusions, but when I've done this before with the MDS Foundation while people are eating, Audrey in the past has said can you just summarize what everybody heard this morning and then, because you can't concentrate and, this way you can sort of go through a little of the stuff that you heard, and it's always nice to hear it two or three times from different people, different ways that people do it. I don't know how lucky you are though that if you haven't recognized, Harry Erba is actually one of the real leaders in the field down here in Alabama. He used to be in Michigan, but the large United States International Randomized Trial that was showing which was his trial and he ran it, so he's actually one of the real leaders in future drug development and in the acute leukemia because I've been asked to give this talk and sometimes they say do the talk from scratch because the leader, the person who gave the talk didn't know what their field is. He's taught me more than I can imagine.

So, just to sort of summarizes and go through again what you heard this morning because sometimes hearing it a little different way, and I'm more of a country bumpkin even though I'm from the big city, I'm down here in the South and I live on the 30th floor in a Manhattan apartment, but I trained at Mayo Clinic and we if you didn't use pharmia analogies, nobody understood what was going on, so when patient first shows up in my office for me to see them for the first time, there's a reason they got there and the reason they got there is because they had either blood counts that were drawn for preoperative for their surgeries or whatever or they were having some symptom, but something triggered the doc to say, hey, you need to see a hematologist.

So on the blood counts, when they do that blood count you saw called CBC that's you've all had a thousand times, every time you go to the family doctor they draw the CBC. There are three and you've heard a little bit about fourth numbers that you pay attention to. There are the red cells and red cells is the red stuff, blood, and red cells, what their job is think of them as nothing more than trucks. So they go to the lungs, pickup oxygen, bring them to the muscles, muscles get fed, you feel good. Muscles don't get fed, you feel tired, you feel weak. Now, there's a couple reasons why my muscles may or may not be fed. If I got a bad heart, I could have good blood and it doesn't get to the muscles and so it's not unfrequent that people have shortness of breath, tiredness, fatigue, feeling run down and the first thing the doctor's doing is sending them to the cardiologist and maybe following up the cardiologist for a long time thinking maybe the pump's not working pumping the blood around, but then it could be also the lungs. If you can't get the air in, you can't carry the blood to the muscles. So, in order for my muscles to feel that they got

enough oxygen and for me to have the energy and the strength I've got to have three things working. I have to have enough heart, enough blood and good lungs, and if any one of those three things is not working properly, the end result is my muscles don't get fed and I feel weak and tired and short of breath and so when we're playing the hematology role, we're paying attention to the blood, but we may have to talk to the lung doctors, maybe we have to talk the heart doctors because what amount of blood the person may need may depend on what the rest of their body's doing.

So, a normal healthy man has 14 pints of blood in their body or basically hemoglobin of 14. A normal healthy woman has 12 pints of blood in their body, or basically a hemoglobin of 12. If you go and you donate blood and you go back to work the same day, you might feel a little fatigued, but you can certainly survive with a pint or two less, but once you hit about 10 pints of blood in your body, hemoglobin of 10, that's when people start to feel tired and the lower they get, the more tired they get. Now, I have people who are at 10 and they really start to fall off the cliff and I have people that go to eight before they start to fall off the cliff. Why? Because the person who's got eight and can do really well probably has a really good heart and really good lungs, but I have some patients that come to see me and the cardiologist calls me and says this guy's got horrible heart disease, don't ever let their hemoglobin get below 10 because then they'll have a heart attack because their heart's bad. So, what number, how many pints of blood you need, is really going to depend on how good the rest of your body is and how good your lungs and your heart are, but we focus a lot on blood, on red cells and the reason is that two out of every three people with myelodysplasia have problems with the low reds as the sole problem that they have.

Another blood count is the platelet. Platelet, their job is to stop you from bleeding. You saw Dr. Erba show you pictures of platelets. Platelets are the clotting cells. You need cells to stop the bleeding and it's not just when you have a big operation. We are klutzes. We bang into things all day and we get little cuts and bruises and things like that that we don't even recognize and I just put a couple hundred pounds of pressure on my feet when I did that and if I had no platelets, tomorrow I'd wake up with bruises all over, but the reason that I'm not going to have bruises tomorrow is because when I just broke a whole bunch of blood vessels with that pound, those platelets have just sealed up those holes, like that. You don't have platelets, all of a sudden they become bruises. Normal platelet count is 150 or more. Surgeons don't mind if it's above 100. They'll be able to operate. But once you get below 100, the cuts start bleeding even longer. Fifty is where we start to get a little nervous, 20 we get very nervous, 10s people bleed a lot, and you saw our last speaker talked about don't bleed and she read on the score. What does that mean? That's serious. That means when you get up in the middle of the night if you have low platelets, we tell people turn the light on because unfortunately I lost a patient who tripped and fell in her bathroom in the middle of the night and the next morning they found her. Now, she could have lived a lot longer if she had not tripped and fall. So, it can get that serious if your platelets are that low, but as long as they're in or above the 20 range, we can feel that the person isn't not going to bleed right away.

And then the third cell is the white cell and the white cell is the one that fights infection and there are lots of different kinds of white cells to fight different kinds of infection. Normal white count is 5,000, but you heard us talking a lot about neutrophils which are 4,000 of those 5,000 and they are the bacteria fighting cells. They're the ones that do the day to day work, the soldiers that fight the infections. The other 1,000 are lymphocytes which are sort of the spies, the T-cells that find infections and the generals, the B-cells, the ones that memorize all the battles and make antibodies so you don't get the same infection twice, but if you don't have enough bacteria, you don't have enough soldiers, it doesn't matter how good your spies or your generals are, and so that's why we put attention so much to neutropenia. How many bacteria, neutrophils, do you have? If you have supposedly 4,000 and you get down to 1,000 of them, that's not a lot.

Now, it turns out that people with MDS don't get as many infections for 1,000 as a person with acute leukemia or chemotherapy for breast cancer or colon cancer. If you had normal white cells and all of a sudden you push them down from chemo, for breast cancer, those patients can get a lot of infections as soon as they hit the 1,000 or 500. MDS patients for some reason the immune system sort of comprises, so even at 1,000 we don't see as many infections as we do for other diseases at 1,000. It's just a weird phenomena that's been seen in MDS patients.

But that's blood. Red's for energy, white's for infection, platelets for bleeding. Okay? And that's what they see when those, every time you go in and get the CBC.

So, a person's sent to me for MDS because they have low one or two or three of those and the next thing I'm doing is I'm sticking a needle into their backside, called the posterior iliac crest. Why? Because you make blood inside your bones, right? If you think about what a dog bone looks like, that's what your backside looks like. It's harder on the outside, hard on the inside and a red core in the middle. That red core is called marrow and that's where you make your blood. When you were a tadpole, before you were born, you made it in your spleen and your liver, but by the time you're born you're making it inside your bones and actually you're making it mostly in your backsides and a little bit in the breastplate and all the other bones are now scar. That's where you make your blood, so we stick a needle in there and we make a diagnosis from that. You don't have enough stuff on the shelf. Right? You don't have blood over here, let's look at the factory. So you'll stick a needle in your hip, look at the factory and in myelodysplasia the problem is the factories are broken. So, under the microscope we can see that they looked abnormal. Dysplasia means change. They've changed their shape, they've changed the way they look and their damaged and basically you've got damaged factories. They're not making blood and that's what MDS is in the simple term.

There are other reasons why people don't make blood that are not MDS. There's aplastic anemia, there's a whole bunch of other diseases, but in MDS you see the factories and you see that they look damaged and that's what causes the disease. Now, why do they get damaged? Primary/secondary, which you've heard about. Could be just out of the blue, primary, or

secondary they had chemotherapy for breast cancer last year and now they've damaged the bone marrow. So if you know a cause, that's a secondary. But there's lots of reasons, but environment and age seem to be the biggies. You all saw Dr. Erba saw almost nobody under the age of 40 gets MDS unless, as in New Jersey, they've worked in the oil industry. So, I occasional have patients who come see me because we have big refineries in upper New Jersey, that's why is smells so much and they get damaged with that then they can get MDS. Robin Roberts got breast cancer, got chemotherapy, years later she develops MDS, that's a secondary cause, but we see the damaged bone marrow. Now, once you damage your bone marrow and it doesn't make blood it can damage the red factories, the white factories, the platelet factories, two of them, three of them, so MDS is not one disease. It's multiple diseases depending on which factories are broken and how many factories are broken, and so when we start to talk about the next thing I do after I've looked under the microscope and said this is MDS is I start to think about the prognosis and the prognosis is going to be dependent on what's broken and how many of them are broken and the fancy IPSS scoring system, if you think about it, a person's going to live a lot longer if they just are tired than if they're tired and bleeding and if they're tired, bleeding and infected, they're not going to do as well. So, the more factories that are broken, the more trouble the person can get it, the worse is survival and the new revision of the IPSS-R is how deep are they broken. We used to say if they're broken or not. Now, we're saying if they're broken a little bit, that's better than if they're broken a lot. So, when I see a patient for the first time I'm going to look at, you know, is this MDS, is it broken-looking bone marrow, but then which is broken, how much is it broken, and how many are broken.

Now, MDS can do a weird thing. You've got your garden and you've got a red plant and a white plate and platelet plant and they're all trying to make their blood and now they're damaged, so they're making less, but every tenth patient something bad happens because as the bone marrow gets damaged and damaged and damaged and damaged, it gets worse over time. This is a progressive disease and that's one of the bad things we have to tell people with MDS is it gets worse if you don't do anything about it. This is all if you don't do anything about it. Over time those factories continue to shut down and in many people with MDS that's the whole disease is that the bone marrow just sort of disappears over time and the blood counts go down over time. In some people, every tenth person, they're going down like this and then all of a sudden they go off a cliff. What happened to that person? Well the white cell factory became a cancerous leukemia blast like a weed in a garden. So you could have plants that are dying away and you have a few weeds, no big deal, but if you get a lot of weeds, it doesn't matter how good the rest of the plants are. How many weeds before the garden gets in trouble, 20 percent. If you got a bone marrow that's filled with 20 percent weeds or 20 percent blasts then it doesn't matter how good the rest of the factories are, and that's when we change the name from MDS to leukemia. So, MDS can evolve to leukemia. It doesn't have to. Some people will just have a few blasts, a few weeds in the garden and they never grow and it's just really how long are they going to live and how well they're going to do is really depending on how fast the factories, the other plants disintegrate, and in some people it's going to be determined by how fast the blasts take over. So once again, when we look at it under the microscope we're counting the number of leukemia

blasts or how many weeds are there to figure out is it likely those weeds are going to take over the garden and how fast they're going to take over the garden and so in the IPSS scoring system, you saw a number of red, white or platelet, how many of those are the trouble? The other next thing we look at is how many leukemia cells. The more leukemia cells, the worse the prognosis.

And then the last thing that Dr. Erba talked about was genetics. We can look inside those cells at the gene level because inside every cell of your body there are chromosomes, there are genes that tell that cell to grow into an arm or a leg or a blood cell, and if those genes are messed up that might tell the plant to disintegrate at a faster or slower rate than the other. Chromosome 5, if that one's broken, the long arm of that, it actually tells is to break and disintegrate at a very slow rate and those patients do very well. Chromosome 7, if that's broken, it's going to disintegrate very quickly. So, when we see the person in the beginning we look at chromosomes to give us an idea of how fast this whole bone marrow is going to fall apart and so when you look at the number of factories that broken, and deep they are, the number of leukemia weeds that tells us how much, how fast the bone marrow's going to disintegrate and the genetics to tell us an idea and from that we can put people into buckets of good risk, which is called intermediate, low risk, intermediate 1, intermediate 2 and high risk and now on the IPSS we have a very low risk category, so we now have five categories instead of four and so you may see on the doctor's chart them write MDS subtype this, what the subtype is basically what the pathology saw, but then the most important thing is then the next line. The risk category was low, intermediate 1, intermediate 2 or high because that's telling us how fast the guess is that this may disintegrate.

Now, from a practical standpoint … Does that make sense so far? Okay. So, that's one of the things you need to know from your doctor is what's my IPSS scoring system. Where am I on that spectrum because that will tell you how, give you an idea and Dr. Erba showed you some not so encouraging curves of survivals based on that. In other words we can make some projections. The curves he showed were mostly without therapy because that's how we… that's how we then figure out where we are and then we look at if the therapy's going to modify that.

Once you figure out the IPSS scoring system the next thing you want to do is you want to start thinking about the treatment. So, I'll have a person come in, we talk to him, you have MDS because under the microscope your marrow looks bad, now let's talk about the prognosis. Well, your prognosis is how many broken factories, how many leukemia cells and genetics, and now that we have that information, let's talk about the treatment. Now, if somebody has a low risk disease, they only have a broken red factory and so they're very tired, but they don't have leukemia cells, they don't have bad genetics. Well, they're probably going to live for a while. Yeah, they may be tired for a long time, but they're going to live for a long time and so in that low risk category, what's going to be my goal of treatment for those people? It's probably going to be to make them feel better by giving them more energy by working on the blood to get the energy up, but I'm not worried about them living and dying because that's not their problem. On the other hand if they have all the factories broken, they got bad chromosomes and lots of leukemia, I know that the IPSS is going to say that they're going to die fast, and so what's my

goal of therapy there? Chemotherapy, poison, get that bone marrow fixed again because otherwise it's too late. So from a practical standpoint, after we do this IPSS scoring system, we really think of patients on two groups, lower risk disease, higher risk disease. Lower-risk disease, improve their blood count so that they feel better. Higher-risk disease, work on the cancer part of it because other wise they're not going to be around very long, but one's quality, one's quantity and they're very different and you have to understand what is your doctor talking to you. If you're talking transplantation, that's to cure somebody. That's aggressive therapy. It makes people really sick. I am a transplanter. I do that for a living and those patients really suffer, but they're doing it to try to become long-term survivors. I'm not gong to offer transplants to the people over here that are just low risk. That's what Dr. Erba was trying show you with those colored parts. Where's the right time? If somebody's just anemic and they're just tired, why would they want to walk in the hospital and have a one out of three chance of not walking out? Because that's the number I tell people. One out of three chances you're not going to walk out of the hospital if you have a bone marrow transplant. On the other hand if you are facing death because you've got a horrible aggressive disease, you take that chance because if you don't, it's over anyway. So, that's these hard decisions you have to look at what is goal of treatment.

Once you sort of get an idea of where you goal of therapy is then there's lots of treatments and to sort of summarize what Dr. Erba said and then I'll go into my talk, there are lots of different ways we can treat this depending on what's broken and what we're trying to do. For many people the only thing that's broken is that they're not making red cells. I think we heard that around the room and the first thing we do for people with low red cells is we give them a blood transfusion. Right? Give them a blood transfusion because you can at least make them feel better right away, they can breathe, they don't have chest pain, they can function. How much blood do you give depends on how much they need to do, how much they want to do. One of my favorite patients from years back, he would come in, his wife would yell at me and say give him blood transfusions, he's just sitting in the chair all day and then she would walk out of the room and he would say, "Don't waste the blood on me, I'm happy in the chair," (laughing) but I also have a young lawyer who's a patient of mine who we're keeping his blood counts almost normal with a lot of blood, more than I would ever think about doing because he's still practicing and he has to, and he told me once if, "I don't have the energy level of the guys who are a little bit younger than me, I'm going to lose my job." So, how high, how much blood I give, how much is going to depend on what the person wants to do, how much you need to do, what the heart doctors are telling me, what their functional status because it's quality there.

There are downsides to blood and we're going to talk about that in a little bit and Dr. Erba talked a little about the problems with too much blood and the iron that's in part of it. We'll talk about that in a few minutes. That's my real slides.

The next step, if it's low red, is a fertilizer. The factories are dying, put some fertilizer down, and we have fertilizers to make the bone marrow grow. These are called growth factors and they come in different brands. There are the red fertilizers, the white fertilizers and the platelet

fertilizers. The red fertilizers - Procrit, Epogen, Aranesp. Those are the common ones, those are the brand names. There's Epogen, he gave, they gave generic names which you guys know the brand names when you walk in the door and the purpose of the fertilizer is to make the red cell factory grow. Now, Dr. Erba pointed out that you can predict who it's going to work on. If my kidneys where I make Procrit normally, my job, I have kidneys that tell my body to make blood. If I cut myself and bleed on the floor, my body knows that I'm a pint short and so how does it know this? Because my kidneys say, Dr. Goldberg, I'm supposed to, my kidneys are saying to myself, I'm supposed to have 14 pints of blood and I only work on cleaning 13 pints. So, the kidneys then send a signal to my bone marrow saying make more blood. That signal is Procrit. It's a natural chemical. It's already in our body.

So if we give people extra Procrit, extra Epogen, extra Aranesp, these are all the same chemical, long-acting, short-acting, one company's versus another, but they're all the same type of chemical that will tell the bone marrow to make blood. Now, sometimes when people have MDS in the beginning and their blood counts are low, their kidneys are already hyper-functioning. They're already chugging out. So, if you already have fertilizer on the ground, what's more a shot going to do? It's going to waste a lot of money, but it's not going to help you. So, that's why Dr. Erba talked about checking the IPO level before your start treatment to find out is this person's kidneys already hyper-functioning and therefore the shots are just a waste of time.

Another reason is if the factories are already dead. If you've got a dead plant, all the fertilizer in the world ain't going to wake it back up. So, once somebody's needing blood transfusions all the time, you think the Procrit's going to really help? The fertilizer, there's nothing there to work on. You got to fix the factory, not just fertilize it. Neupogen, these red cell fertilizers are just fertilizers. They're not fixing the factory. We have drugs to fix the factory and I'll talk about that in a second, but when we talk about Procrit and EPO and Aranesp, we're thinking about things just trying to fix the… just grow the factory more, but if the factory is broken, they won't work. So, they tend to work early on from when somebody's first diagnosed to get them started. Now, the other piece is, and I've seen this unfortunately done and I've even made the same mistake myself. I've had people who are doing well and all of a sudden their blood counts start to fall again and saying, "Well, what's going with the Procrit? why isn't it working anymore?" Well, you still need iron, you still need vitamin B-12, still need folic acid. It's sometimes actually you work the chemicals are working and then you just run out of all the other things that the cell needs. So, before I start abandoning a fertilizer that was working, I want to go back and make sure they have all the other vitamins they need. If you were making cakes really well and all of a sudden you ran out of flour, even if you have all the other ingredients, you still need the flour. So, it's possible sometimes people were doing really well with the fertilizers and all of a sudden the counts dropping and it has nothing to do with the factory disintegrating. It has to do with the fact that they ran out of iron, they ran out of folic acid or ran out of B-12. So, you go back, think about that. So, that's actually a type of question that you may want to have your doctor, I've been getting Aranesp, it's not working anymore, it's not working as well as we wanted it to, do I have all the other ingredients? Because if I don't have all the ingredients then it's not working,

but if you have all the ingredients and it's not working, well maybe it's time to start thinking about fixing the factory.

Now, just we've talked a lot about the Procrit's and the reds, but there are fertilizers for whites, Neupogen, Neulasta. These are drugs that will make the white counts come up a little bit, but as Dr. Erba said we don't generally recommend using them chronemically, but we use them when somebody gets an infection. If someone comes in with infection and you say, "Look, I need the immune system to kick in right now, couple shots of that, you'll get a temporary boost. That'll get you through the infection." There are some studies and actually you saw him show a slide, of two fertilizer may be better than red (inaudible 27:02). So sometimes even if it's just a problem with the red, before I abandon fertilizers and move to fixing the factory if they were doing okay on it, I might add a little bit of white cell fertilizer and there have now been several studies including one that Harry actually chaired. He was being honest that if somebody was going okay with the red cell fertilizer like a Procrit and it's not working, adding a little bit of Neupogen, in very tiny doses because there you're not really trying to boost the white cells, you're just trying to tweak that red cell fertilizer a little bit better and that sometimes helps kick a person back up.

And then there's a platelet fertilizer. That's been more tricky and that's not standard care at this point. There's been some concerns about the platelet fertilizers actually moving people towards leukemia. There was a recent report actually recent by just a couple weeks ago that may be Promacta may actually be able to do this without making the risk of leukemia, but this is where we're researching. So, we've got good red cell fertilizers and white cell fertilizers for MDS. For platelets, it's still no man's land. We don't really have the sense. So, that's the fertilizers.

If that's not enough and the factories are disintegrating despite that, we then have to start to have to think about fixing the factory or if you had aggressive disease from day one, you weren't waiting around from we're thinking if you have leukemia cells in there, putting fertilizers ain't going to help. You need to… so if you have an intermediate 2 or high risk, you want to think about more fixing the factories, killing the weeds, stimulating the plants, and there we have three drugs you heard. First drug Lenalidomide, brand name is Revlimid, it's a pill and it stimulates the red factories to grow. Purely for the reds. That's why we only use it for the reds. In fact it may, as you saw slide that from Dr. Curtin's slides, that it actually may make the whites and platelets a little bit worse, but it will bring up the reds in some people. It will bring it up on most people if they have chromosome 5 broken. It will bring up about a quarter of the people if they have other genes that are broken. So, we actually know that there might be a group of people that that pill works on, but that's purely for reds.

Then we have two other drugs that are both giving either through the IV or through a shot. One called Vidaza, Azacitidine, and one called Dacogen or Decitabine. They're Coke and Pepsi. They're both hypomethylating agents. Hospital will use one, hospital will use another. They're essentially the same type of drug. Yeah, there's a difference between Coke and Pepsi. There's a difference between Vidaza and Dacogen and that's where your doctor can use a little skill, but

for the most part they are both drugs that basically stimulate the bone marrow in two ways. They kill the bad cells and stimulate the good cells. They're really kind of interesting in the way they do that in that they glob onto the DNA and they glob on a little bit it stimulates it. If they glob on a lot it kills it and it turns out the more angry and ugly the disease is the more it globs on. So, it actually will stimulate some good cells while it kills off the bad. So, we think about Vidaza and Dacogen when we have a couple different… and these are given through in the IV or through a shot one week a month and it can be five days a week, seven days a week. If you live in Cleveland it's six days a week. I mean, everybody has their own little schedules of how they give one week a month, but the bottom line is that you do this and it slowly turns the bone marrow back on while it's killing off the bad cells.

If you have a person who's got low red you might start with a Revlimid first. Give it a shot for two months. If they have low whites, Revlimid doesn't work. You have to move to these shots. If you have low platelets you got to move to the shots. If you got leukemia cells you got to move to these shots.

We know and Dr. Erba showed you that doubling the survival two years that these medications improve survival. Remember, I told you have a goal of therapy. Early stage disease you're trying to make people feel better. Advanced disease you're trying to make them live longer. Vidaza and Dacogen have shown to improve survival. They bring up the blood counts and they keep the leukemia cells from taking over the bone marrow and people live longer. Every so once in a while I get somebody who comes to me, a family member usually and as we're talking they pull me aside and say, "Look, you're not giving Grandpa chemotherapy," and I said, "Yes, I am," and they say, "But my cousin got breast cancer chemotherapy and she was sick as a dog." These drugs are weird. They make people feel better while they make them live longer. They're not what you think of as chemotherapy because they're doing two things. They're pushing down the bad cells. That's the chemo portion to make them live longer, but they're stimulating the good cells. So, the red cells go up and their energy gets better. So, in a large international study which it did show they actually looked at not only did the people live longer, but the quality of life was better in the group that got the chemo compared to the people who just got blood transfusions. So, this is the one time I tell people don't be scared of chemotherapy because the chemo actually makes you actually feel better than if you just decided with transfusions alone. These shots once you start them, though, you do one week a month for the rest of somebody's life. So, it really is a big decision of when you say a blood transfusion here or there, a little pill versus now you got to be seeing me all the time, one week a month for the rest of your life. That's a hard decision. It may not be a hard decision if the marrow says do it, but if somebody's just having a low red and their energy is falling and Procrit's not working, well, is it better to just give them a blood transfusion and see them once every two months or is it they're in the office all the time maybe I should be giving them something else to try to fix it and that's the art of medicine there.

That's the standard treatments. Bone marrow transplant, way over here, aggressive, aggressive, aggressive. Now, you're saying look, let's just replace the whole bad bone marrow with a good

one. So, in a bone marrow transplant or stem cell transplant or a hematopoietic… whatever you want to call it somebody goes in the hospital for a month. They're out of commission for six months to a year at least. In MDS patients who are over the age of 50, one out of three of them will die from the treatment, ie. I kill them with the poisons. One out of three of them I don't get rid of the disease, but one out three of them I cure. That's the numbers. That is their scary numbers but if you don't have much choice people take that risk. A 50 year old like Robin Roberts is going to take that risk because she's younger, she's healthier, she's probably not going to have as much chance of dying and she wants to get 30 more years. A 75 year old may say I don't want to take that kind of risk. Give me blood transfusions and keep me going for a little bit longer. That's where the hard decision is because a bone marrow transplants not a fun procedure.

That's the standard stuff that you heard already this morning. There's one or two other little dinky ones I would mention especially since I heard immune type people in here that there are some other problems with your immune system. We certainly see people who get myelodysplasia have a higher… people who have immune problems like rheumatoid arthritis and those type of things and receive those medications have a higher likelihood of getting MDS and we're not sure if it's the underlying disease or the treatment because even before Enbrel came out, even before other drugs came out people with rheumatoid arthritis got MDS at a higher rate. It may be the person. If their immune system can attack their joints, it can also attack the bone marrow and it turns out that if we look at different gene called HLA-DR15 that you were born with, that's a gene that people are born with as opposed to the genes that are in the cancer cell. There is a higher likelihood if you're DR15 that gene that you're going to get rheumatoid arthritis and there's also a higher chance that you will actually get MDS and it turns out that people work from the National Institute of Health if you're HLA-DR15 positive then there is another set of treatments that are available that MDS Foundation is actually doing the study and that is can we give people horse serum or Campeth. Basically, knock out their immune system, reboot it just like… I got a problem with my computer, I'll just turn it off start all… let it start from scratch. Sometimes we will take people with immune based MDS, turn off their immune system completely with horse serum really like Mr. Ed. Blood from a horse and you inject it into a person. It turns off the immune system, but then when the blood's gone that horse blood is gone the immune system re-turns on and sometimes you can actually see the patient with MDS almost be cured. It doesn't happen very often. It's not a very common therapy, but it certainly is in the literature. It's certainly something I've done. Actually, I talked to Harry afterwards. He's done it. We've all done it, but we have to have the right setting of a little bit of a younger person with a history of rheumatologic diseases only with a bone marrow looks a little funny and it's sort empty-ish marrow and they have the right type of gene, HLA-DR15. If you have all those things lined up but then you think this is the right way of therapy and that's actually something that a high end hematoblast to do this all the time. It's not something that most… It's in all the text books and nobody thinks about it, but whenever I hear somebody that says, "I have a history of rheumatology," if I have a rheumatologist I can draw an HLA-DR15 to see if that's pointing in the right direction.