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Sandy Kurtin, RN, MS, AOCN, ANP-C

Sandy Kurtin: ... get started so you guys can go on to enjoy the rest of your day and I know several people had to leave because they're heading back to LA in parts where the traffic is particularly challenging. It's hard to sit for this long, so we understand that, but what we'd like to do first of all Dee just passed out a survey so if you can take minute to fill those out. That would be very helpful. It gives us information that will help us plan other kinds of programs for support and so we take this information very seriously and it's helpful to the foundation to help us understand how best to help you. So, why don't we just take a couple minutes to fill that out and then we can open up discussion and questions.

(General conversation 1:05 – 2:25)

Dee: I'll probably E-mail this form to the people that left. So if you get it again and you already completed it, don't worry about it. You don't have to (inaudible 2:34).

(General conversation 2:35 – 3:58)

Sandy Kurtin: Okay. Why don't we go ahead while everybody's finishing up? So, the rest of the afternoon, the next hour, I think we have or however long it takes is really just to open it up to all of you. Is there something you heard today that you don't understand? Is there something that we didn't address? Is there something... (Attendee)?

Q1: So, the medicine that is available can be very expensive. Are there opportunities to not have to spend so much money and get help?

Sandy Kurtin: So, the question is first a comment is is the medicines are very expensive. That is very true and depending on your situation it may be something that you can or cannot afford to do and the question was are there resources to help you and yes, there are and in the *Building Blocks of Hope*, I should have one of those binders handy for here. There is actually a segment there and I believe it's the Seeking Treatment. It's actually the big binder that gives you a list of assistance programs. So regardless of where you are, if you... what my suggestion would be is to ask for one of the social workers in some... It is in book five. Okay. So, sorry. I wrote this thing and I can't remember where it is. So in book five apparently under My MDS Plan it will give you... there's an insurance reimbursement resources for family and caregivers, specialty pharmacies, additional researches. So page 28, 29, 30 and 31. So, there are a number of resources available. We use them all the time in our clinic to help people with the out of pocket expenses or if you're on a limited income. There's paperwork involved and people have to assist you in completing some of those applications, but there are resources out there. Some of them on the Health Well Foundation there's something that is replenished once a year. Once the money is gone for the year it's gone and then they'll start up in the new year, but it's... but you can ask about it. The first thing you do is to ask and there are usually in every clinic people or a person who is the point person to help in that process. So definitely ask about it. So, that's a very good question.



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Okay. What other questions... anything that wasn't clear that you don't understand that we didn't answer or didn't talk about? Other questions people have? Yes.

Q2: (inaudible 7:08) some of the treatments they shouldn't use over the counter treatments. If you have a low white count (inaudible 7:16) still use is the (inaudible).

Sandy Kurtin: So, that's a very good question. So her question is over the counter medicine. So in general, over the counter medicines, herbal medicines, alternative therapies, anything that you're taking, the first thing you want to do is really talk to your healthcare provider about that. Nonsteroidal anti-inflammatory things like Advil, Aleve which was your question specifically are really the hardest on your kidneys and as we get older our kidneys don't work quite as well and you can end up with some problems with your kidneys don't work quite as well and you can end up with some problems with your kidneys. So, that's the most important things about those drugs specifically. They aren't just hard on platelets as people think they are. They're not even close to aspirin which if your platelets are low we tell you no aspirin. So, there are a million different scenarios with over the counter medicine. The best thing to do is just bring a list with you and this is why the MDS plan is so important because you can put all of that information in there and you can basically online download individual pages if you have the ability to do that or you can make copies of these blank pages so that it's expandable and then you just take it with you to your visit and it allows you to say, "Here's where I'm at," and I know people that are very organized that my patients who can figure out what's going on way before I can find it in the chart because they're keeping their records current and that really helps us do the best thing for you as the writers. So if you take sort of the time and make the list of medicine including over the counter, any herbal medicines. There are some things that we'll tell you not to take because they might interfere with your therapy or we don't know enough about them and they can be toxic to the liver or the kidneys. So, it's just tell everything whatever it is you're taking, no judgment. Just say, "You know what? This doesn't go with that," or this might be harmful to the kidney or liver, kidneys or liver, and the important part about that is that any of the therapy that we give needs to be processed through the liver and kidneys. So, it's important to us to keep all of your organs healthy and you healthy like I spoke earlier and so that there's no... we're not excluding any treatment down the line. So in order for you to have that bone marrow transplant, for instance, your kidney function, your liver function, your heart function have to be ready. You have to meet certain criteria. So, over the counter drugs, herbal medicines, supplements of any kind can make a difference and we need to talk about that. I just tell people bring them in, we'll look them over and I'll tell you yes or no basically based on what we know.

Q3: One thing (inaudible 1:15) is about (inaudible) especially about blood transfusions (inaudible 10:21) but there is a shot that you could (inaudible 10:27). I don't know if it works for everybody, but I don't get any other blood transfusions and I don't have to do it. I get a shot every couple weeks and eliminates (inaudible 10:36).

Sandy Kurtin: So, the shot that you're getting it is in the book. So, there is... Mostly everything's in that book. I know because I put it there with the help of many people, I have to remember, but there is a segment on transfusions, but what you're describing and he did talk about it are the erythropoietin what we call erythropoietin stimulating agents or ESAs and those are Procrit or

Aranesp and they are basically erythropoietin, that hormone that's in the kidney that you take an immature red blood cell to become a mature blood cell and carry oxygen. So without that hormone you can't make red blood cells or you can't mature the red blood cells. Most people with MDS have plenty of their own, but there are a group... so if you're... He showed the slide where if you had a level that was below 100 you would do the best. Medicare and the people that authorize these shots in order to qualify for reimbursement for payment your erythropoietin level has to be below 500 in order for you to qualify and that's because we know if it's above 500 you have plenty of your own and giving you more is not going to help you. It's not the answer. So, there are a group of patients who actually do very well on Procrit or Aranesp over a long period of time. They tend to have low risk MDS and have not required that much in the way of transfusions. So, that's probably the case for you if it's working and that's great.

Q3: A little bit higher risk. It works for me. I understand it doesn't work for everybody.

Sandy Kurtin: No. So, that's good. Yes.

Q3: It just happened to save me from... otherwise, I'd be living down (inaudible 12:24).

Sandy Kurtin: Exactly and that's not...

Q3: (inaudible 12:26)

Sandy Kurtin: So, that's good for you. That's absolutely true. Okay. What other questions, comments... (Attendee)?

Q4: So, if you go through stem cell transplant there's a whole bunch of things that can happen and there's opportunity to succeed, there's opportunity for it to not necessarily to work. What happens when it doesn't work? Is there another opportunity to have a second stem cell transplant?

Sandy Kurtin: So the question is about cell transplantation which to date is the only potential cure for this disease. It's important to understand that in MDS you cannot have your own bone marrow. So, in myeloma, in lymphomas, we use autologous, your own cells. We collect your own cells, we clean them up in the lab and we give them back to you. In myeloid malignancies, MDS and acute myeloid leukemia you can't have your own cells because of the way those things happen that Dr. Bejar explained this morning. So, you need an allo transplant, allogeneic which means somebody else's bone marrow. That bone marrow can come from a sibling. That's our first choice because there's going to be less of a potential for that bone marrow to fight with your body or it can come from an unrelated donor. We call that a MUD, a MUD transplant, matched unrelated donor. Depending on... and then there's a match game. So, you have... there's eight original matches. You can go as high as 10 and what this tells us is that these markers that say 'I'm more like you than not,' the more of those that match the better that is, the less likely you are to have problems. So, we talk about 10 of 10 match at the highest level. If you're a 10 of 10 then the good thing is is that you're going to have a little bit of this... what we call graph versus disease. So, the bone marrow when you get somebody else's bone marrow it is the immune system and by some miracle they infuse it... It's like a blood

transfusion. Those cells find their way into the bone marrow and they set up shop and they start making all kinds of blood. So white blood cells, red blood cells and platelets. Essentially that becomes your new immune system. That immune system they say, 'You know what? I don't really like this body. This house is not for me,' and you have this sort of constant struggle and that's why people that have allogeneic stem cell transplants need to be on drugs to suppress the immune system so that that marrow and your body get along. So, they call that graft versus host and but there's a good part of it is that in that same process keeps the disease from coming back. So, I'm getting to your question. So, the idea is is that the closer the match the more likely it is to take so that the cells set up shop successfully, you have a new marrow and that's good. That process of back and forth can cause some illness and in some people make them quite sick. We can get through it a lot of the times, but there is a lot of the risk and if you are considered for a transplant, they will have that conversation very frankly with you, risk versus benefit. It's not a simple process and people can feel pretty sick for a while. I personally have MDS patients who have had transplants who are for all intents and purposes cured and as far as we know the disease is gone because they got somebody else's blueprint. You know, your chromosomes are your blueprint. They're what tell your cells to become a this or become a that. In order to get rid of the bad blueprint which is MDS, younger a new one and the new one you get is somebody else's bone marrow. If you fail the bone marrow transplant, you can have a second transplant and sometimes they will do that. They will also sometimes use infused white blood cells from the donor. So, they'll save those and give those back. It's a little boost to try to get it back under control, but the question after failing a bone marrow transplant 1) is are you well enough to do it again, how long has it been and 2) can you find another donor because that donor that you just had obviously wasn't the answer. So it becomes a little bit more complicated. Is it done? Yes. There are people who have more than one transplant. So, that has happened. Those tend to be younger patients.

Q5: Is it true that very seldom anybody who's 60 can get a bone marrow transplant.

Sandy Kurtin: So, the question is anybody over 60 which is really quite young, I might say, can have a transplant. So, it used to be that way. We used to say if you get your own bone marrow, the cutoff was 65 or 70. We now do auto transplants, getting your own marrow in people that are in their mid to late 70s because it's a lot like just some of the chemotherapy we give for certain diseases and people actually do very well so that you don't have that graft versus host problem. It's your own cells, so people can do actually really well, but again you can't have an auto transplant in MDS. So for an allo transplant because this of this whole graft versus host and the intensity that's needed to treat you ahead of the transplant you need good kidney, liver, lung and heart function. You can't have any chronic disease that's out of control and this is where we get back to be healthy, take care of yourself. If you do have diabetes, hypertension, any of those things, you get it get tuned up. So, we got to take care of the whole you not just this little bit with MDS. Your whole you has to be well because that's going to make you do the best you can with the transplant. Then you need a donor. So, the best donor is a sibling. So, how many people that you know are 75 have a healthy, living sibling donor? Kind of hard to come by and I have a patient who 72, was the oldest of 12 children. Lucky for him and he's had one of his younger siblings that was actually a perfect match and we did an allo transplant and he did well. Most people don't have one of 12 siblings and they're the oldest. So sibling donors present the least risk in just the whole process of the transplant itself and then you get to the unrelated donors

and then it all becomes about the match. So if you're 70, in great shape and we have these people, we will consider it, but we will consider it depending upon the level of match. So, we aren't going to be doing like two (inaudible 19:44) mismatches where two of those 10 or two of the eight if people go by eight aren't connected or aren't good aligned because it substantially increases the risk and as we get older our organs, the ones that I just discussed, don't repair themselves as well and so older people are just prone to having function that's not quite as good as when we were 50. Does that make sense? So, there's a lot that goes into evaluating a transplant candidate and deciding whether they are appropriate for the process.

Q5: (inaudible 20:23)

Sandy Kurtin: It's very risky. I mean, it's a big deal. An allogeneic transplant is not an easy process. We get people through it and they do okay, but there is a risk of toxicity that's substantial for everybody. There's a risk of death by the procedure itself and so when you go to transplant evaluation they will go through that with you in detail for you specifically looking at all the things we just talked about here's what we think your risk is and here's what we think your potential benefit is and then they will say, "Is this what you want to do?" So, it's a very open in-depth discussion. I'm going to go here and then I'll go back over here. You raised your hand?

Q6: Yeah. If you have a sibling and it would be like an eight out of 10 match and then you had a nonrelated donor that's 10 out of 10. Which would they...?

Sandy Kurtin: So, that's a very good question. So the question is if you had a sibling who's an eight out of 10 and you had a matched unrelated donor that's a 10 out of 10 what would you do? Very good question. So then it becomes are they young? Male? Let's say they're a young male. I will say this to people, "You know what we need like a young male football player," but then I look at the (inaudible 21:36). Those people aren't so smart sometimes, so let's choose a golfer, well somebody, anybody. A young male is probably the best match you can get because they've never had a child and so once you had a child so your other choice is a female who's had children. They've had exposure to other chromosomes in the baby because that's that exchange that goes on. So if you have two siblings, one brother, one sister, regardless of how they got along as children, we would choose the male sibling probably because they'd be least at risk. Then they'd look at how healthy is that donor, whether there are things going on, what's their family history. When we do donor evals, we go through all of that and we say, "You know what? I'm not sure this person is a good donor." So, that would be the first question with the sibling. Then you would say, "You know what? There's something to this graph versus leukemia, that graph versus disease that's important for long term outcome," and in those cases if that 10 of 10 match is a perfect match and they're a good donor they may choose that donor knowing that if you at some point do need a second transplant you got a sibling match down the road. So, there's a lot of thought that goes into this. It's not that simple to say it's always this or that. It's about evaluating the donor and evaluating you and it's very complicated and it isn't the same for every person. Does that answer your question?

Q6: It does. The female hasn't had children?

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Sandy Kurtin: Then they're pretty equivalent, but you go through the kinds of questions they ask in terms of deciding on a donor. Yes?

Q7: A sibling versus somebody else (inaudible 23:24). The other question is how long does stem cell (inaudible 23:29)?

Sandy Kurtin: You mean the graph versus host or graph versus...?

Q7: We have struggles to get through it.

Sandy Kurtin: So the first part of the question is what about nephews, etc. down the line. The further you get away from your actual gene pool which is your mom, your dad and their offspring, the less likely you are to find a match. So, we don't generally use donors like a parent to a child because in a way it's a different... they come from their parents. So by the time you get to you it's not exactly the same. Cousins are a totally different gene pool unless they have the same father, which we don't recommend.

Q7: (inaudible 24:15)

Sandy Kurtin: Pretty much. So once you get away from your immediate family, it's really unrelated in that... I mean, they're related, but they're not first generation relatives. How long does the struggle go on? It's so incredibly individual and so much of it has to do with how well is your disease under control before you go to transplant. So, the question earlier why wouldn't you go straight to transplant if you had a donor? Well, we know the people that do the best have their disease under some kind of control. It's not out of control because the transplant preparation is just basically big doses of chemotherapy and some radiation in many cases and if your disease is not under control that is more work to do and then you put a marrow into that environment it may not do as well. So, you have to have well controlled disease and then the other one is how well are you otherwise? And this is the whole key about staying well. If you go into transplant not being well you're not going to do as well as the person who's fit and otherwise healthy and that doesn't mean you can't have diabetes or hypertension. It just means they're under control.

Q7: Like what's the (inaudible 25:29)? Is it six months? Is it a year? Is it two months?

Sandy Kurtin: No, there's no way to get a number because it's all individual. There are people who struggle for a long time, years, a couple years. There are people... I would say everybody has some pretty intense probably until... we have this day 100 where we kind of do an evaluation for people. So basically three months. That's pretty intense. That period of time for allo transplant. They can stay that way much longer, six months, nine months, a year. It's highly variable, but it's an intense process for everybody in those early months which is why we have the evaluation process that we do.

Q8: (inaudible 26:17) if you have your match, your donor match, but you don't need the transplant yet. How long will that take before you have to (inaudible 26:24) blood again (inaudible 26:26)?



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Sandy Kurtin: So if you have a match if you've been evaluated for a transplant and they initiate a donor search which is worldwide. So, a national marrow donor program is worldwide. They basically look everywhere and so we have many people that find their match in Europe or South America or wherever it is depending on your ethnic background and once they've identified a match that donor is... they sign a thing that says I'm going to be available, but it's not forever. We've had instances where the donor gets pregnant and they say, "You know what? I won't be available now for 12 months because I'm going to have this baby and I'm going to need to recover." So, the donor isn't there forever because they're volunteers and so they don't normally do that search unless they really think they're going to move forward to transplant, but they can... those donors can be released after a certain period of time they release the donor.

Q8: But I thought they take that (inaudible 27:28) from their bone marrow.

Sandy Kurtin: Nope, not until they...

Q8: I thought they freeze it or something.

Sandy Kurtin: No, no. That's an auto. So if you're having an auto transplant where you have your own marrow, you can collect it and store it for later.

Q8: But you don't with the other one.

Sandy Kurtin: No because these are volunteer donors and they're not making cells and they're waiting on a shelf somewhere. They have to actually donate their cells in a very short period of time prior to the transplant.

Q8: And let's say you need it or let's say you have a match and then about two years later they (inaudible 27:59) and all of a sudden you need it...

Sandy Kurtin: That donor is going to be long gone.

Q8: He might be gone?

Sandy Kurtin: Oh, yeah.

Q8: Does that mean you got to go through the blood work again to find out....

Sandy Kurtin: Absolutely because those people aren't just going to sit there and wait for you.

Q8: (inaudible 28:11).

Sandy Kurtin: So this is why the transplant process is so formal and complicated because we have people getting their body parts, their window as a volunteer and that has to be recognized and

appreciated and so they're not in limbo. So if you... so they normally do not even test you unless the thought is you're going to go forward to transplant.

Q8: So at the end of '13 I did mine because I thought I was going to have to have it in the beginning of '14. If I had to do that now, my donor might not be there anymore?

Sandy Kurtin: Yeah. That's true. You can be tested for yourself. You can be typed, but if you are initiating a donor search...

Q8: I mean, they know if my donor is still out there. Right? If I needed this now in the next two months, transplant is my donor is still there.

Sandy Kurtin: The donor can change their mind. There's nothing in here that says they can't say no thank you. Before they take you to transplant that's why they do it a week or 12 days or whatever it is before you're due and they say that donor, if you... we're going to move forward and if you've committed doing this and you back out at the last minute this person might die. So, they make the donor say very seriously, "Yes I'm going to go through with this," because you don't want to end up treating someone and not having the marrow to rescue them. So, it's a very formal process. Yes?

Q9: This is off the bat topic (inaudible 29:46). You had mentioned that in going to the stem cell transplant, of course, you get the dose of the chemo and sometimes radiation. What qualifies for radiation treatment?

Sandy Kurtin: So, we used to do total body irradiation in big doses and that's to get rid of all the lymph nodes and the other part of your immune system that would potentially reject the new marrow. So, you're basically eradicate or clearing out your own immune system to make a new one and so now they do more an abbreviated version of that. We used to make people just incredibly sick with the TVI which is what it's called. So, they still do some form of it, but it's much lighter and a lot of it depends on the donor's source. So, sibling versus MUD in terms of amount and it's usually done all in one day, the TVI. It's like a single dose that they do in one day where there is a few other ways to do it and the level of radiation that we would get was much more intense. So, it may differ for each individual person based on the goals and the donor source and your age and many things. If you're very young, they're going to go full (inaudible 31:01) and that's generally the plan and... but even then we don't give what we used to give. We've gotten smarter about it and the technology allows us to do better. Yes?

Q10: How do they hide the (inaudible 31:18) how much volume do they need to (inaudible 31:20)?

Sandy Kurtin: So, very good questions. So, they harvest the marrow. There's two ways. We can do peripheral blood stem cells. So, the stem cells are those little cells... If you remember Dr. Bejar's slide, that little cell up in the left hand corner. Those are called CD34 cells and they basically have the ability to self-renew and replicate and make the whole complement of blood. So, that's what we need. You can get them in the peripheral blood. You put a catheter like a Hickman catheter. It's like a tube in your chest. We give you growth factor. So, the things we used to make white blood cells

increase and they give you a lot. So, it pushes numbers are really high and then you... a little machine collects the cells and they take... it's a pretty phenomenal thing. It's like the white cells go this way and everything else goes back to you. So, that's one way – peripheral blood. The second way is your bone marrows and they basically take you to the OR and you all had bone marrows. I've done about 12,000 of them in my career. I have a little callous right here, but I'm pretty good at it, but you go in the OR because they take as much as they can and sometimes it's as much as 500 ccs. So when we do a normal marrow... not always. They can't always collect that amount. So, there are multiple punctures and multiple aspirates. So, they knock you out for it basically. So, there are bone marrow stem... there's bone marrow cells and there's peripheral stem cells.

Q11: Does one work better than the other?

Sandy Kurtin: You know, there's a lot of discrepancy. For a long time we got away from bone marrow and went to peripheral stem cell and there was some... There's still discussion about long term outcomes and it varies by disease. So, there's still some people that believe peripheral stem cells are different in that they matured somewhat and they... so, they have the ability to move out and you may... and so the difference becomes in how much of this graph versus disease effect are we going to have. Now, these are donors. These are not you because you got a donor. Right? But to take a donor to the OR and put them under anesthesia is more risky than doing a peripheral stem cell. So, it's balancing risk and benefit and what you believe the long term outcome will be and part of that comes from how close the match is. So, it's all part of that whole decision process. So, it depends is the answer. It's not one answer unfortunately.

Q12: How come the blood cells (inaudible 34:07) from the stem cell?

Sandy Kurtin: Because they're fully matured cells. So, they're completely programmed. They're only going to be a red cell. That's all they get to do. When you get a transfusion, they're temporary. So, they don't have any renewal capability at that point. Stem cells can make new cells. Red blood cells once mature that's all they get to be when they grow up and they have a short lifespan – 120 days and then they're gone. When they're transfused like I give a unit of blood and you get that unit of blood, those red cells aren't going to last 120 days because they're borrowed. They've already had some time. So, they have a shelf life, if you will. So, it's temporary. The stem cells are a factory. They make new cells. Totally different. Yes?

Q13: What kind of side effects are associated with MDS chemotherapy?

Sandy Kurtin: Side effects with MDS chemotherapy. So, we don't use chemotherapy per se in the true sense of the word so much anymore. There are some drugs. We use some low dose Cytarabine or Ara-C sometimes. In transplant, there's a big dose of chemo that goes before the transplant to clean the marrow out completely and the regimens vary by institution, sometimes by age, but the... so Azacitidine and Decitabine are technically hypomethylating agents. They target this CPG island which is an element on the DNA strand and the protein that's there. So, they're technically not really chemotherapy but close. Revlimid is an immunomodulatory agent. So, it works in a completely different way on the bone marrow and so they're very different. The side effects vary by drug. So for

the hypomethylating agents for all of the drugs, anything we do in MDS the most common side effect is myelosuppression, the ravine. You need them to do that because that's where the MDS is. In order to make it better we got to get rid of the bad cells and in that period of time, you're going to have the other ones. There's collateral damage. They're going to affect some of the normal cells that are going to drop. So, myelosuppression, 100 percent across the board, the most common side effect of any treatment for MDS usually temporary and hopefully your marrow will function better and then you'll get better. The other things for the hypomethylating agents. So, Decitabine and Azacitidine, Vidaza or Dacogen, you might know better, are the other terms for that. Nausea and vomiting usually we can control that very well. Constipation not fun. A lot of people claim the things we use for nausea and vomiting which mostly are Ondansetron or (inaudible 37:04) what we call H23 inhibitors, but the reality is it's probably the hypomethylating agents. So, I ask my people all the time and talk about it because then you're going to want to do something. You need a bowel regimen, a stool softener at least plus or minus a laxative. I'm a firm believer in good old MOM, Milk of Magnesia. It's cheap and works great. You can take it every day no worries, but you don't want to be constipated particularly if your platelets are low because you can bleed. So, that's a big thing. Azacitidine can be given as an injection and sometimes people get injections reactions. There's a way around that. Something called the air sandwich which is in your binder. You might share that with your staff. Those are the biggest things for those drugs. Revlimid, myelosuppression also. Very little nausea and vomiting. People can get a rash. That rash is not a true allergic reaction. It is because it's an immunomodulatory agent which means that my (inaudible 38:07) system and you have immune cells in your skin and because of that they're sort of stimulated and people can have rashes that come and go. So, we usually treat through that unless it's very severe. It can cause some low thyroid over time. So, we check that and what else? A little bit of probably irritation in the gut. So, probably diarrhea if anything and those are the most common. Yes, and those are all highlighted in book five, Seeing Treatment which I think is... I think it's book two.

Q14: (inaudible 38:44).

Sandy Kurtin: No. It's really considered immune therapy or (inaudible 38:53) therapy. It's an immunomodulation agent. So, it works very different than standard chemotherapy. Okay. What other questions? How about you guys down here at the end of the table? Yes.

Q15: (inaudible 39:06) could I try Procrit again?

Sandy Kurtin: So, there are people who after their disease has been treated in other ways can be re-sensitized to Procrit and this is true particularly of people that have been on Revlimid over a period of time. There were actually some trials done to look at people then going back to the erythropoietin agents, the ESAs like Procrit or Aranesp and being sensitive to them again. So, it's a possibility. In order to get the drug though, you have to meet all the criteria which is a low EPO level, you have to have iron, B12, folate all completely corrected. You have to have less than five percent blasts and only in that instance will Medicare and most other insurance companies actually pay for the drug. So, yes it's possible, but you need to meet that criteria. Other questions? Yes.

Q16: I think they say Vidaza is considered chemo?

Sandy Kurtin: Not really. It's kind of different, but it's close.

Q16: So one of the side effects is chemo brain (inaudible 40:21)?

Sandy Kurtin: So chemo brain is an interesting phenomena. So, there're actually people that are truly recognizing this. There's a great guy. He's out of Harvard, Cory Dietrich, and he's done a lot of research in terms of neurocognitive just meaning how we remember or don't remember changes on chemotherapy and there is a real phenomenon. Most people don't completely understand what happens or how to fix it. If you talk to a neurologist, so he's a neurologist at Harvard. If you talk a neurologist, mostly they will say to you there's a certain amount of forgetfulness that comes just with age. There's a certain amount of forgetfulness that comes when you're just tired all the time. When you're really, really tired you can't think as well or concentrate as well for as long. There's a certain amount of it that probably is related to drug effect and that part we don't understand as well. There is no (inaudible 41:23) or magic wand to get rid of it quickly.

Q16: Darn.

Sandy Kurtin: But I tell people if I had (inaudible 41:30) I would share it with you, but what they will tell you and there's no quick pill to make that better either. There are things that people suggest or talk about that are used in Alzheimer's, but we really don't have... It's a whole different process. Most people tell you to work your brain and so a lot of the neurologists are now recommending Luminosity. That puzzle game online which I have had patients tell me it's really very frustrating just to have you use that part of your brain that is just memory and recognition and so it's an area like fatigue where we really don't have all the understanding on this thing, but it's probably more than just one thing. Other questions people have? Things you want to... We had conversation about the whole experience with having MDS.

Q16: So with the Vidaza, you know it's not chemotherapy. It's typically done in a hospital environment. Is that for the safety of the patient or is that for the safety of the medical personnel?

Sandy Kurtin: No. That's probably because the drug is very unstable. So once mixed, it's only good for two hours. In the original trials, they did it in a way where it could be self-administered. That's why the oral Azacitidine people are really hopeful that that will move forward. So when we give Vidaza in our clinic, we don't make the drug till the person is there and we know they're good to go because you're going to waste it. It's only stable for two hours once mixed. So, it's purely pharmacokinetics.

Q17: Is the oral available?

Sandy Kurtin: It's not commercially available. It's in trials. The original trials what they found was that people have a lot of side effects. So, they sort of went back to the drawing board. Most of the work is being done out of MD Anderson. Dr. Garcia Manero and his colleagues and the trials are being run in different places, but they kind of went back and reformulated things and it seems now to

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be better tolerated. So, the trial going on right now is comparing that to your regular administration. Is it doing the same thing? So, what we call a non-inferiority trial, but one thing is not inferior to the other. So, the route of administration could be oral and the idea is that you come every month for seven days is a huge commitment because it's never quick.

Q18: You probably go back from (inaudible 44:07).

Sandy Kurtin: Yeah. We do this all in our clinic as an outpatient, but that means you got to drive in every day from where you are, you got to check in, you got to wait. Our clinic is just like every other clinic. It is not that efficient. There's always something that comes up and then what should have taken an hour can take three and it takes a huge amount of your time and we're aware of that. It's just that's the way the drug is available right now. So hopefully, the oral compound will come to fruition and be approved and be an option for people. If you're on subcu or IV Azacitidine, they'll have to chop it up, switching over to an oral at that point, how does that look? If you have not benefitted from subcu or IV it's not likely the drug will work any better than the other routes. So, that's an important thing to keep in mind. Yeah.

Q19: Why would a doctor instead of the seven day therapy, why would the doctor ever achieve a five or even a three day?

Sandy Kurtin: Okay. So, the original trial for Azacitidine was done using seven consecutive days and so purists like Lucille Ramen (sp? 45:20) who did the original trial compared to trend and Aaron Makos (sp? 45:24) who's my colleague who's on the (inaudible 45:26) with me will... that's the way they saw the best response. There was then a trial then right after (inaudible 45:35) that compared five versus seven just trying to say our clinics aren't open on the weekend. What do we do about Sunday if you are open on Saturday and he did this evaluation where they did five two days off and two. They did five two days off and five. So, 10 doses or they did the original seven and what they found in that study which was mostly low risk patients, you have to understand or lower risk, is that five was equal to seven. We know now is when you go back if you dose reduce to five, it's a 33 percent dose reduction off the top. Now, MD Anderson who sees a lot of... probably more patients, them and Moffett, probably the two largest programs in the country had said there's people that can actually get away with three or four days, but those studies are very small. So, most of us will have there on seven for as long as it takes to actually have a very good response and usually that's nine months or a year and then they might be willing to go to five just because we're not trying to get you to spend all your time with us and we feel pretty comfortable in keeping that response under control. So, this is where you'll see people move to five. We don't start anybody on five unless they really have to have counts, in my setting, unless they have bad counts and we're not sure we can get them... we need to get them through it. There's a lot of variables there, but mostly we start with seven because we need to get the disease under control.

Q20: (inaudible 47:15) heard the dosing change with Vidaza, I think, low cellularity?

Sandy Kurtin: Dosing change if you have low cellularity. So, this gets to where the marrow... what are the reserves. So, your normal cellularity should be 100 minus your age. So if I'm 60, my

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cellularity should be 40. Most patients with MDS are hypercellular meaning that their cellularity is higher than it should be, but there are people who have hypocellular. So if the marrow is pretty empty MDS and what... so then we say okay, what is the bone marrow capacity to recover? So if I know this marrow has to do all this work, make red blood cells, white blood cells and platelets and it's pretty empty and I give chemo and I'm going to put it in a ravine and I'm already halfway down the way what is my reserve and so there are people who will modify doses based on marrow cellularity where you have to really be sure is that it was a good sample. Marrows are not marrows. You got to look at the actual sample. Was it a good marrow? Did it have the right cells to evaluate? Was the bone core good, so that you can really say with certainty yes it's hypo cellular and then you make a judgment. So, we don't do that routinely off the bat because some people do well and that hypo cellularity is a reflection of the disease and we still need to treat the disease, but we aren't going to just push forward forever knowing that it's down. Now if you've been on therapy a long time and you become hypocellular, that's a different story. So, start versus later it makes a difference. Any other questions? Too much information. I know. There's a lot of possibilities.

Q21: So, the use of Vidaza like in my husband's case, we're waiting for a transplant, but he's (inaudible 49:18) multi (inaudible 49:19). So, it's going to take a lot of (inaudible 49:22)

Sandy Kurtin: Hard to find a donor.

Q21: How long has Azacitidine been successful? In other words, is it like a 12 months and then it starts to kind of wane in its efficacy?

Sandy Kurtin: It's completely individual. Lou Silberman will tell you that the longest patient that he has treated and he's probably used the drug more than anybody in the world has even out five and six years. That's not the norm just like Chet is not the norm, but it can happen. If you look at the literature, it's pure just estimate of the average which nobody is average. So, there are people that do better or worse. They will tell you 24 months. I have people that have exceeded that, a number of people that have exceeded that. I have people that are on cycle 39 and 40. So, they're beyond the 24... cycle 24 which would be two years. So, it just is variable and a lot of it has to do with the initial characteristics of the disease, how long has it been there? As you heard earlier, it just sometimes takes a long time to be diagnosed and so that is... the timeline is ticking. So, there's a lot of variables that go into that, but we don't ever stop Vidaza once we start unless it's become too toxic because the way the drug works in suppressing those (inaudible 50:47) we talked about, hypomethylation. When you take the drug away that will all start back right up and it can actually sometimes move in a more aggressive manner. So, we treat until unacceptable toxicity or progression. So, people should be on it until he goes to transplant is what we would do and I think that would be the standard of care. Other questions? Thoughts? Things to share? (Attendee), in the back. She's got lots of questions.

Q22: Well, some of them I already know the answer and I'm just sake the asking the questions in a group sense, but so you just said something to me that went "Uh oh." Is there ever a reason they would take somebody off of Vidaza knowing they're going to put them back on but maybe like four or five months later?

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Sandy Kurtin: We would really hesitate to do that because we know the physiology. We negotiate. I mean, there are people that say, "You know what? I just need a break," and then they'll stay out one or four months and we'll say, "Okay..." Just like if ever you seen the picker show where they (inaudible 51:57) the amount of money. My husband watches this and they'll say, "Okay. I'll give you 700," and they guy said, "No, how about 500." So, we negotiate and we think about. So, taking six weeks off is a whole lot different than taking four months off when you know the physiology of the disease because in people who have failed Vidaza, truly failed, which unfortunately people stop without failing. We know that the disease then tends to behave badly. So knowing that, we try not to give them too much untreated time, but we negotiate because... and that's balancing toxicity, time, money, patient wishes. I mean, people get to decide what they want to do. We'll not going to force you, obviously. We're not going to drive over and drag you out of your house and come get your shot. So, we... it's a discussion that has to be had. Yeah?

Q23: Something I heard recently. We don't fail the transplant. We don't fail the treatment. The treatment fails us.

Sandy Kurtin: Exactly. Very, very... So, what he said very, very important. You don't fail anything. The treatment fails you. So, that's a very important thing. It's nothing that you did. It's just that our treatments are not perfect and so the transplant can fail, the treatment can fail you. It's a better way to phrase and you have to be aware of that when we talk because it's true and sometimes they just don't work and we are limited and the good thing is is having been at the ASH meeting, for years I try to go every year and hear people from all over the world talk and there's some really smart people working very hard to figure things out, but it was a very hopeful and uplifting meeting in terms of MDS because people are figuring it out. New targets, new pathways that we can exploit to treat the disease. So we should be hopeful in every way. Dr. Bejar is one of the... He seems like a really unopposing, nice guy. He's incredibly smart and he has done some of the pioneering work in MDS that's going to move us to the next phase and so there's this young group of guys mostly, some women, who are way, way, way, way, way, way smart and they're... I mean, just wow. Like they must have other conversations when they're together that we would not understand, that I understand and I understand a lot and so it's exciting. So again, the trick is stay well. Try to keep things under control. I can't talk about wellness enough. So, that the (inaudible 54:49) they will be coming and I really firmly believe that. It's been a long time coming. Yeah?

Q24: So, do you arrange (inaudible 54:58) international?

Sandy Kurtin: Yes.

Q24: Do they have a different protocol somewhere else in the world? In Europe?

Sandy Kurtin: Oh, yeah. Yeah. You know, for every disease there is not consensus and so depending on what's being studied, but I have to say in the MDS community and I've been in this group and I call them my peeps, they're my peeps. It's a very close knit group of researchers, nurses, statisticians. It's a family. Wouldn't you agree, Audrey? This is a really close knit group because years ago there were probably... I don't know, maybe 15 experts and now we have many, many, many, many and we

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have Centers of Excellence all over the world and they is that you do build consensus and that you can have a consistent approach to treatment. It isn't too hard to do in MDS because we only have three drugs and in Europe they don't have all three in some places. In the rest of the world, they don't have access to all of these drugs necessarily. So, they may see different things there. We're lucky in the United States. We're rather spoiled when you look at the world as a whole when it comes to medicine, but I think the ideas going forward is having this kind of consensus group at MDS Centers of Excellence, the International Working Group in MDS. Now, the Molecular subgroup of that that there is consensus across the world and then you have all these brilliant people sharing ideas and that's the goal. So, we have our MDS International Symposium that will be held in Washington, DC and there's a patient forum connected to that. Right, Audrey?

Audrey: Yes. It'll be on Saturday, May 2.

Sandy Kurtin: Saturday, May 2 in Washington, DC and so we'll have patients from that region, obviously, but possibly from other places and that meeting is only MDS experts. The whole meeting is dedicated over four days just to MDS. So, all the people from all over the world will come together to say what are we doing, where are we going, what's next and how do we get this done? So, it's exciting.

Q25: (inaudible 57:10).

Sandy Kurtin: A lot of it is posted. There are sections of it that will be available on the website. The posters are published in the *Leukemia* magazine. I do believe they're accessible through the MDS Foundation website. So, a lot of it might be more than you... I know you're already going, "Whoa, man. My head is so full," right now. So, some of this gets to be way too complicated but we all have in the newsletter sort of a summation of what does that mean to the real person. So, you might look for the newsletter through the MDS Foundation as a way to sort of translate all that science into what does that mean for me and then we will, obviously, update the *Building Blocks of Hope* to reflect anything that is a significant change in practice.

Audrey: If I could add that Dr. Gore in the organized (inaudible 58:12) that (inaudible 58:13) agrees to recheck everything. So, it will be our Fall newsletter that will have a synopsis of everything that was covered during our symposium.

Sandy Kurtin: We should challenge them to put that in what is this... if I'm a patient who could I say that in simple, understandable terms.

Audrey: I'll encourage Dr. Gore.

Sandy Kurtin: We should say that is his... You tell him I challenge him to that outcome.

Audrey: I will.

Sandy Kurtin: I'll tell him. I'll send him an E-mail.



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Audrey: You tell him.

Sandy Kurtin: I will. It's hard to get the... I mean, it's hard for us to understand all this, but trust me. I mean, I (inaudible 58:51) constantly and it's hard for the general person and if you're seeing a practitioner that's in a community and they see breast and lung and colon and prostate and everything else, I mean, the science is just so crazy, good crazy good, but to keep up with it all is really tricky. So, we need these Cliff Notes and cheat sheets for everybody but at different levels. So, none of us can learn that.

Q26: So, it's not in the newsletter?

Sandy Kurtin: What's that?

Q26: Is it published in some kind of newsletter?

Sandy Kurtin: You can access it online through the MDS Foundation. It's free. You can get it. It's for you. So, we... There's a way you can check with Audrey.

Audrey: In your *Building Blocks of Hope*, the newsletter is included in there and I believe Sandy was our guest editor. She did a wonderful story on transfusion dependence and it actually is great, but yes, in there will be information how you can join as a member and we have your information now. So, you'll all be in the database. You won't have to join. You'll be in our system now, so don't worry.

Sandy Kurtin: Okay. You have a question. Yes.

Q27: You may have mentioned back on (inaudible 1:00:11) all that well, but is there anything that you heard about this really (inaudible 1:00:19) about the clinical trials other than making the medication that (inaudible 1:00:28) oncologist wouldn't be aware of?

Sandy Kurtin: So the question was are there any really (inaudible 1:00:38). So at ASH, remember I tell you it's the side of hematology. The MDS Foundation hosts a symposium every year and part of that symposium is to talk exactly about that thing and it's been a long time since we've had that level of excitement and to have people like Alan List who's one of the founding fathers, if you will, of MDS and Steve Nimer and Ryan Cusolon (sp? 1:01:03) who's out of Philly and Pierre Pinot and others talk about the level of excitement in these new compounds was amazing and so, yes, there's hope. It's probably... They're only available through clinical trials at this point. Those clinical trials are not available everywhere, but I would encourage you if you're interested or have questions to call the MDS Foundation. There's nothing wrong with you as a patient or a caregiver taking something to your doctor saying, "Hey, do you know about this?" and I will sometimes say, "You know what? Can I have that? I'm going to make a copy," because I don't always know everything and so there's no reason for you not to say would this be okay for me? There's no reason you can't go onto clinicaltrials.gov and look up MDS and it'll spit out available trials for you on the computer and/or



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call the MDS Foundation and ask about it because we always recommend clinical trials. That is the only way we get new drugs. It's the reason we have the three we have today is because people were in trials that are required to get them approved by the FDA. So, we always recommend a clinical trial. You can always do standard therapy anytime, but clinical trial... we try to never exclude a treatment option. So if you're here and I have two choices and one's a trial and one's a standard therapy, I'm going to say you know what if you meet the criteria for the trial let's do that first because I just come back and do this whenever I want however I want, but this trial might only be open right now for you and so it should never be saved for the very end. We used to do that and we don't anymore. We move them way up in the scheme of things. So, it's good to find out what's out there and whether that's a good option for you and whether it's feasible for you to get where you need to go to get the trial. That's the tricky part because they're not available everywhere. Other questions you guys? Yes?

Q28: (inaudible 1:03:07) question. Revlimid gets dispensed 28 count and yet we take it every day. So, why is that?

Sandy Kurtin: Because Revlimid comes under the REMS program which is basically a reconciliation and mitigation of risk program that is run by the FDA because it is an analog of Thalidomide which caused birth defects when the drug was given in the '60s and those things have not been found in Revlimid, but we don't want to find them. So, you can only get 28 days at a time.

Q28: It doesn't mean that you can't get...

Sandy Kurtin: You can't get refills. They won't give you 30.

Q28: But you still need to take it every day.

Sandy Kurtin: Right. You need to take it every day, but they will not give you more than 28 days at a time because of that risk you have to answer all those silly questions and...

Q28: So is it advantageous for us not to use it three or four day (inaudible 1:04:04)?

Sandy Kurtin: What do you mean?

Q28: I mean otherwise, you wouldn't give it in the full dose.

Sandy Kurtin: No. You have to just order a week ahead of time to be able to get it on time. We don't want you skipping doses.

Q28: So, it's a paper thing not a...

Sandy Kurtin: It's a paper thing. It has nothing to do with science. It's purely mitigation of risk on behalf of the FDA. There's no science involved. It's just paper. You're right. It's a process.



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Alright. Any other questions? I know it was a long day for everybody. If you have other questions please call us, let us help, really look into your book five as a tool for you to guide you with the health and wellness and keeping track of your counts and all of those things. We wish you all the best and let us know if there's things we can do better. We take that to heart and with that I will let you get on with your day. Thank you very much.

(Applause)