



Speakers: Elizabeth A. Griffiths, MD
Elizabeth A. Griffiths, MD
Sheila Tighe, NP

MDS Foundation: ... some quality of life and empowerment discussion. I also want to say one more thank you and goodbye and thank you to United. My flight's leaving a little earlier than I originally anticipated. So, I'll have to leave before the end of our program, but thank you so much for everything today. If you have any other questions or there's anything that the MDS Foundation can do for you please do not hesitate to reach out and ask. Thank you.

(Applause)

Sheila Tighe, NP: Hello. Thank you for having me. So, we're going to talk about our patient and caregiver guide for living with MDS.

So, what are our treatment triggers? This is especially important in preventing or delaying progression of MDS to more serious forms of leukemia such as acute myeloid leukemia. So, what are our treatment triggers? Transfusion dependence. Does someone get transfused once a month with some red cells and then all of a sudden their counts drop and they're here three times a week? Progressive or symptomatic cytopenias meaning are you having recurring infections because your white blood cells are low? Easy bruising or bleeding because of a low platelet count. Fatigue needing naps throughout the day. Shortness of breath from a low hemoglobin or weakness. Increasing blasts. This is indicative of disease burden. As your blasts increase in your peripheral blood we can assume they're increasing in your bone marrow as well and high risk disease. Median survival is only about one year.

Individualized treatment strategy is key. The number one thing we look at is performance status. Good versus poor, fit versus frail. Performance status actually describes a patient's level of functioning in terms of their ability to care for themselves. Daily activity, physical ability. Can they walk into clinic? Is someone wheeling them? Can they dress themselves? Do they need help with their activities of daily living?

Comorbidities. Do you have heart disease, kidney disease, lung and liver disease? Next, we look at the revised International Prognostic Scoring System. This rates three factors – percentages of blasts in the marrow, chromosome abnormalities that Dr. Griffiths talked about and blood counts.

Degree of cytopenias. Lower risk disease. What we want to do is we want to improve hematopoiesis. The formation and development of blood cells with low risk intensity treatments such as growth factors or hypomethylating agents such as Vidaza or Decitabine. These are given in the outpatient setting and typically have lower risk profiles.

Higher risk survival and primary versus secondary MDS. Secondary MDS are those patients who have already been diagnosed with a cancer in the past and have been exposed to chemo and/or radiation therapy.

Lifestyle. Does someone want to play golf? Do they want to be out shopping and whatnot? Is this going to be an inconvenience to come to our clinic seven days a week, get transfused three times a week and just personal choice?

So, allogeneic bone marrow transplant remains the only potential cure as Dr. Griffiths had said. It's not an option for many. Age plays a factor. Usually those patients less than 60 years old do well. Comorbidities. Again, heart disease, lung disease and availability of a suitable donor. Patients of a Caucasian race are more likely to find a donor and does someone have a sibling donor? Age alone should not exclude active therapies. What's most important is that we look at patient's physiological age. This tells us a patient's kidney, liver reserve. So, again we look at performance status. Is someone out jogging three miles a day or are they in bed more than 50 percent of the day, comorbidities and again, fit versus frail.

All active therapies for MDS require time to work and will continue indefinitely if they are working. Four to six months of continued treatment is required to evaluate effectiveness. Normally we don't even repeat a bone marrow until after the end of cycle four of therapy. Blood counts often get worse before they get better. We need to plan ahead, set expectations. Some people want to travel to Florida for the winter months. We can do that. We just have to arrange for blood transfusions down in Florida, Vidaza to be given in their outpatient setting. Proactive management of side effects in the early phases of treatment is key to obtaining the best response.

So, why is time required? What is really happening? So, before treatment begins blood counts drop as MDS progresses. Normal blood cells are crowded by abnormal stem cells in the bone marrow and blood. So, I always try to tell my patients it's kind of like having children at home. They're in your space, they're using your water, your electricity, they're in your way and they're not paying any bills. So, weed them out. When treatment is initiated treatment cleans the marrow, blood counts may drop further, patients may experience hematologic toxicities. So, what are those? Your platelets drop, you have nose bleeds, gum bleeding, neutropenic, you have an infection. As the patient begins to respond the bone marrow begins to recover allowing it to make healthy blood cells. Blood cell count should rise and symptoms of MDS should improve. As the response continues patients can be weaned from supportive care as robust response sets in. So, as someone's responding they may have to come to clinic three times a week for blood transfusions and all of a sudden you see their counts respond. So, ideally they come for seven days of Vidaza and you don't see them for three weeks in between. The challenge is getting through the first few cycles. Early toxicities may be difficult and are discouraging for the patient. Some of those are nausea, vomiting, loss of appetite, constipation, fatigue. Some people come in and say oh my God. A truck just ran me over. I don't know what to do. Painful injection sites from Vidaza. There's lots of things we can do to get through all of these symptoms.

Key principles of therapy for MDS. Time is required for the best response. A minimum of four to six months. Cytopenias, meaning low blood counts, often get worse before they get better. Strategies for getting through the initial cycles of therapy. Setting expectations, knowing this is going to be a slow process. I have to hang in there. Ninety percent of the battle is mental. I got this. I can do this. Dose modifications or delays. Your fatigue is profound. So, you discuss with Dr. Griffiths maybe we delay

your next cycle by one week. We dose reduce your Vidaza. Symptoms become much more tolerable and supportive care.

So, this is the response chart following four cycles of Azacitidine. As you can see you fix the factory and your counts become better and here's a chart for the patient response over 10 years of Lenalidomide therapy. It's sustained moderate but asymptomatic cytopenias, a new normal. So, your white count may not be normal from 10 to 14, but it's in the two or three range. So, you have neutrophils to fight infections.

So, becoming a partner in your care. Building your MDS plan. My MDS Manager. So, tools and strategy for success. Maximize each treatment option. Become a partner in your MDS journey. Caregiver self-care. Those that are taking care of us need to be well. Ask for help. I can't do this alone. Look at your friends, church members. I need rides here or there. Stay well. Build your MDS plan. Explore the *Building Blocks of Hope*. So, there's an app called My MDS Manager. This enables patients to track and store relevant health information between clinician visits. Features and electronic journal. Tracks your symptoms, lab results all in one place, medical history. We'll constantly ask did you have a heart attack? Do you have high blood pressure? Some people say I don't know. It's all in one spot. You don't have to worry about it. Patient education. It has links to MDS, acute myeloid leukemia right on there and it helps you track your care team. So, if we say to you you saw a kidney doctor. Who was it? When did you see them? It's all right in one spot.

What can I do to maximize each treatment option? Understand your disease. Know your IPSS and your Revised IPSS score. Learn about your blood counts. Hemoglobin, white blood cells, absolute neutrophil count, platelets. Ask for copies of your lab results. When we see our patients copies of labs are the first thing we hand out because you'll be the expert. You'll say my hemoglobin's this. It fell this many grams last week. I don't think I can go a whole week without coming in for a transfusion. Take medications as prescribed. If you come in and you say you're having symptoms and we're trying to optimize our medication plan and then you come back a week later and you say I'm still having diarrhea. Did you take the Imodium? Did you do this? Did you eat a bland diet and you say no it's kind of like starting at square one again. So, we want to maximize that plan. Keep your appointments for visits and for treatments. That's most important when your counts drop. If you need transfusions and your hemoglobin's already a low level and you miss a couple appointments it's going to be that much lower when you come in and you're going to feel that much more fatigued. Ask about symptoms that need to be reported immediately. If you have no neutrophil count, a fever of 100.4 can be a life-threatening infection. Patients need to get IV antibiotics within four hours of that fever. Track your symptoms. I get my Vidaza on this day. I can't move my bowels on this day. It seems to happen every cycle. So, then we can be proactive. Ask about the goals and expected duration of treatment. I always tell people okay you're starting with Vidaza. It's not a quick fix. It's a slow process. Once we start we don't stop. It keeps going and going and going. Ask about financial assistance programs. Some of our medications, our prophylaxis medications are very expensive. The drug companies can offer them for free or get less expensive drug for you. Best treatment for the patient. Shared decision making can help guide patient and caregivers to include individual preferences, goals and values. We can tell you this is the best option for you, but you need to help in that plan because if you don't think it's right we're not going to be successful.

Make the most out of every office visit. Set an agenda for each visit. Ask yourself what do I want to get out of this visit? Write down the top three things you want to discuss because we may get sidetracked. You may talk about one symptom and then we forget about the two other things we really wanted to talk about. Focusing on your agenda will help you make the most of your time. Prepare questions before the visit because it's always after you leave that you say oh, I forgot that one thing and it might take a while to get that answer. A list of questions in priority order. Start with this list and take it with you the next time you go to the doctor. Bring a member of your personal support team to take notes so you can listen. We actually have patients that come with tape recorders. You have to ask the physician is it okay to tape this, you do and then you get to play it back to all your family members. So, 10 different people aren't calling and getting 10 different stories.

Update your provider on anything that has changed since your last visit. Keep an up to date list...

Q1: Your slides might be one off from your talking.

Sheila Tighe, NP: Oh, thank you.

Keep an up to date list of prescription and over the counter medicines, vitamins, herbs and supplements you are taking. This is very important because a lot of our drugs do not study the interaction with herbs. We may not want you to take a simple over the counter Ibuprofen or aspirin because your platelets are low at that point in time. Most of our patients before they're prescribed a drug they call and they say can your pharmacists look at this? Are there any drug interactions? Am I allowed to take this? We say yay or nay. If not, we'll come up with something.

Make notes on symptoms and side affects you are having. Bring any test results from other healthcare professions you may see. Cardiologists. They just did an EKG, a stress test. You come here and you tell us oh, I'm having chest pain we're going to get an EKG. We have if you bring your data we can use that information. Eye doctors, dentists, primary care providers. A lot of the times we have to coordinate with dentist visits. We have to transfuse platelets. You may be neutropenic. It might not be a great idea to get a tooth pulled at that time. You may need antibiotics before or after the procedure and transfusion records. If you go to Florida for the winter months bring back those transfusion records. Let us know what you needed down there, one a month, every three days. Leave the visit with a clear understanding of the plan. Follow appointments and treatment plans. Am I coming back in one month? Am I coming back in two days? What's the plan? Instructions for taking any new or existing medications. Again, that may be drug to drug interactions and any referrals to other providers. We may want you to see a kidney doctor, cardiologist. Symptoms or problems that should be reported. Again, fever, bleeding,

Who to call and where to go. This is extremely important during business hours may be one phone number. After business hours complete different phone number. Who and how to manage the office and system. We have a patient portal here at Roswell Park. You can E-mail any of your concerns. We have to get back to you within 24 hours. Phone calls. If you call our clinic and you leave a message on the machine, I tell patients if you don't hear back from us in two hours call again. Don't ever let that get lost in the system.

True emergencies. Always call 9-1-1.

Caregivers are an essential member of the healthcare team. They need to focus on their needs, too. Maintain a healthy lifestyle. Nutrition, exercise, sleep because if they're run down they're not going to be of benefit to us. Relaxation or meditation. Intimacy or sexual health. Spirituality. Treatment for depression and anxiety. Ninety percent of the battle is mental. I've seen people actually will themselves to die. Once they give up it's a downhill trend. Strike a balance each day. Asking for help. Be specific. Hey, can you make me a dinner tomorrow? I have to be at the clinic all day and that would really be a big help. Cooking, cleaning, shopping, yard work, childcare, elder care, help with driving and these are all things we can ask caregivers for.

So, there's an app called Lots of Helping Hands. It's a painless way to organize help. So, there's an online calendar, you designate a member to be your community leader. What they do is they coordinate the calendar. It only takes minutes to create. The calendar is flexible. Changes can be made. The coordinator adds names and E-mail addresses of friends and families. It lists needs. Again, meals, rides, etc. Someone just to sit with me while I'm at clinic for eight hours. This all goes onto the group calendar. Friends and family check to see what's needed and sign up to help. The calendar automatically sends reminder E-mails to those who volunteer, so I can't forget to bring you your dinner.

What can do to stay healthy? Continue to enjoy things you love. Live. This is the point of our patient therapy. We want it to be a minor inconvenience in your everyday life. Come here, leave and go do the things you like. Ask for help when needed. Lifestyle. Very important. Balanced diet. Sufficient amount of protein and calories. No smoking, limit of alcohol. We actually have patients who can't drink alcohol because their platelets are low and it increases the risk of bleeding. Increases their liver functions while they're getting chemotherapy. Daily activity. Keep up with your walking a mile a day or what not because the more you sit the more you're going to lose. Get enough rest. So, patients will come in and tell me I didn't sleep all night long. But did you sleep all day? Yes. That's why. So, simple sleep hygiene. I say don't take a nap for five hours and you'll be great tonight. Learn to manage and report your symptoms. I have patients who bleed from their mouth for seven days. They come in and big blood blisters and I say when did this happen? Right when I left clinic seven days ago. It could have been much more easy to take care of. Call us when things happen. No question is a silly question. Exercise. The single most important way to combat fatigue. Ask about a referral to physical therapy or trainer or develop a tailored program. Any patient that says I think I may benefit we send a script off, PT to evaluate and treat. They'll come out if you're not homebound we send you to an outpatient physical therapy. They'll give you a program. You do that at home. Strength training can even be done in a chair using resistant bands or lightweight five pound weights, a couple curls a couple times a day. Great. Light cardio such as walking will add benefit. Eat light before bed. Avoid reading a backlit device in bed. Dark quiet and comfortable sleeping. Help your body relax. Again...

Q2: Why do you avoid reading your Kindle in bed?

Sheila Tighe, NP: They just say sometimes the backlight.

Q2: Does what? It sounds like (inaudible 21:08). There's some days I just watch television in bed and backlit devices like the iPad. It's not like the Kindle. The Kindle doesn't (inaudible). If you change your habits. Don't watch TV in bed and don't do what I do in bed. (Inaudible)

Sheila Tighe, NP: Again, if you're not sleeping well talk with your provider because if you are practicing sleep hygiene and not resting during the day or at night that's not good either. There's medications we can use.

Nutrition. Stay hydrated. I often tell my patients drink half of your body weight. One hundred eighty pounds, drink 90 ounces of water per day. People say oh, I drank three pops and this. That's not staying hydrated. That's actually acting as a diuretic. Balanced diet is key. Protein, vegetables. General nutrition guidelines. Get nutrients from food. Avoid highly processed foods, sugary foods, high fat and excessive preservatives. So, all those things that come in a box probably not the greatest. Limit or exclude alcohol intake. Adequate calories and protein. Avoid fad diets. I had a patient who came in and didn't feel well and we couldn't figure it out and he said oh, I'm trying the starvation diet. You eat one thing in the morning and you don't eat for 24 hours. I'm not getting chemotherapy and I'd feel shaky and yucky, too. Ask about any food restrictions. Neutropenic diet most important.

Avoid infections. Monitor you blood counts. Know if you're at risk for infection. This way maybe that week you don't go to church and sit next to the people sneezing and coughing. Avoid people who are obviously ill. I always tell people call instead of coming to see them if you're sick. Wash your hands. Before anyone touches or after they touch you. Talk with your healthcare team about symptoms that need immediate attention. Again, a fever, chills, sweats. Some people get confused. It can be a terrible urinary tract infection and they have no idea. Immunizations. Keep up with your immunizations. Flu shot every year. Pneumococcal vaccine. Make sure you talk with your doctor though because during chemotherapy is probably not the best time. In between cycles. We have to make sure your counts are adequate to get an intramuscular injection as well.

How do I avoid bleeding? Your risk of bleeding may increase if your platelet count falls below 50,000. Talk with your healthcare team about recommendations. You may need more frequent count checks instead of once a week, twice a week just till we get your platelets back up. We tell our patients they cannot use a toothbrush when their platelets fall below 50,000. It has to be soft or we use toothettes. No flossing of your teeth. We don't use a razor. Electric razor if anything. Avoid aspirin or aspirin containing medications. If you are taking any blood thinner, Cumatin, Xarelto, Eliquis, Plavix, Talk with your healthcare provider about whether or not you should modify your medication schedule. I had a patient who said well, my artery is 70 percent blocked and I said that's okay because you'll die taking that Plavix from bleeding to death before that ever becomes 100 percent blocked. You cannot take that when your platelets fall below 50,000. We usually discuss this with the cardiologist, so everyone's on board which is important, too.

Managing comorbidities. Stay connected with your primary care provider and specialist. I know it feels like you're here every day and you think it's a one stop shop. Most of the time we can accommodate that, but let's say you're on thyroid medicine. Someone has to monitor those levels every so many weeks or months they make changes. So, seeing your primary care doctor is important.

Managing each of your diagnosis is necessary to stay well. Keep a current list of providers. Contact information, fax numbers, phone numbers. Share this with each of your providers so they can communicate and collaborate to improve you health. What we do is we carbon copy all of our notes to any physician that you have listed. So, if you've changed a primary care physician three months ago and we're not aware they're not getting any of your medical information. Keep us informed.

Palliative and supportive care for cancer. The World Health Organization recommends that all patients with a life-threatening illness can benefit from palliative care now known as supportive care at Roswell Park. The focus of palliative care is to prevent suffering and improve quality of life. Some people say what do you mean you're sending me to palliative care. I'm not dying. I'm doing well. You just told me to go out and live, but maybe you're constipated every time you get Vidaza and I've tried certain medicines that aren't working. Supportive care comes in and they use their expertise. They say melt a pat of butter on a spoon, take that and you'll poop every time. So, that's what we use them for. Interdisciplinary symptom assessment and management. Focused on both the patient and family at all ages and stages of life is the core of palliative care. Combined terminology. Again, palliative and supportive. We present it as supportive now.

Again, the My MDS Plan, that app. Understand your diagnosis of MDS. The MDS Plan provides several tools to allow you to track and manage your journey. You may want to make extra copies of some of these tools before writing them on so that you can continue to track your progress, but this way when you come to the office it's all in one place.

So, the great thing about this app, I went on yesterday to look, some people forget to take their medicines. They may have to take Zofran a half hour before their chemo. It's actually got a reminder on there and it will alarm and tell you time to take your Zofran so there's no reason to forget. It gives you an opportunity to participate in a virtual support network. So, when I went on there was all these patients asking all these different questions and people responding. So, it was a live talk basically and it gives you live support through the MDS Foundation. This just shows what it looks like.

So, hope. *"Hope is the thing with feathers that perches in the sole and sings the tune without the words and never stops at all"* – Emily Dickinson.

So, patients or caregivers may contact the MDS Foundation. The liaison is Audrey Hassan. Here's her phone number and her E-mail.

So, any questions? Thank you.

MDS Foundation: Does anybody have any questions?

Q3: I think you can hear me. It's a very quick one. With the immunization for shingles because there's a live virus the patient can't take that, but can a caregiver take that and then be near the patient?

Sheila Tighe, NP: Dr. Griffiths? Shingles vaccine? Do you think...?

Elizabeth A. Griffiths, MD: So, (inaudible 30:14) although there's a live (inaudible). So, in general if somebody is very neutropenic we do not recommend that the caregiver get the vaccine and if people do get the vaccine then we say that they should wait two weeks before they're hanging around the person who's got the immunity defect. This is certainly the case for people getting induction chemotherapy. For people who have more profound and prolonged neutropenia like people who have chronic MDS with chronic neutropenia the data is a little bit less clear. So, I don't have a firm answer for you. I think... I don't have a firm answer for you. I don't know the correct answer. I think the general recommendation is not... is for the patient for sure not to get it and probably it's safe for the family member, but we don't know. I guess what I can say to you is they give a lot of that vaccine and I have not seen an outbreak of shingles and most people particularly the shingles vaccine is not very well transmitted person to person. So, it's probably safe. I can't say 100 percent that it's safe, but it's probably safe. Does that make sense?

Q4: I'm hoping it's okay that I just share something for you.

Sheila Tighe, NP: Of course.

Q4: The Resource Center at Roswell has a lot of resources for people. So for instance if you are having trouble cleaning your house there is a company that will clean your house for four months while you're under your treatment. They also have things about the (inaudible 32:27) program which you can get services at the Y for, I think, 12 weeks, free Y access, but a lot of things that I would just encourage you to use and also if you're from out of town they have suggestions for places that you can stay and get the support you need for living arrangements because you might come from out of state. So, I just wanted to offer the Resource Center for everybody because I volunteer there now and can't tell you what we can do for you.

Sheila Tighe, NP: That's wonderful.

Q4: Cleaning the house is a big one.

Q5: Do they charge you?

Q6: I have a question regarding depression. I'm dealing with a lot besides this and I feel like I need (inaudible 33:35) when I try (inaudible) and (inaudible) so I'm wondering if anybody uses anything natural or has any success with any antidepressants that don't drop your blood counts.

Sheila Tighe, NP: Anybody?

Elizabeth A. Griffiths, MD: So, one really effective way of combatting depression can be exercise. (inaudible 34:04) There's actually (inaudible) of people who have depression done very well is a regular exercise programs (inaudible) in the absence (inaudible) individual (inaudible) for people who don't have tolerance (inaudible) there are other types of (inaudible). There is also (inaudible).

Q7: The exercise is very, very effective and my wife who has cancer is the one who likes to exercise. So, I had to make a deal if you hold my hand I will walk with you, but seriously my love for her is what gets me to override anything. Romance at Roswell Park.

(Applause)

Sheila Tighe, NP: Does anybody want to share their MDS stories because most people it comes out of nowhere. All of a sudden they're feeling fatigued or they go for a pre-op evaluation and the doctor says your counts are abnormal and oh, my gosh you're off to Roswell Park or an oncology center. So, if anyone wanted to share their story.

Q8: Sheila, doesn't vitamin B12 help our mental states?

Sheila Tighe, NP: I don't know that it... Dr. Griffiths, vitamin B12 mental state?

Q8: As far as depression.

Elizabeth A. Griffiths, MD: So, B12 is an essential building block (inaudible 36:14) and (inaudible) if you have a B12 deficiency people can feel very rotten (inaudible) most of us (inaudible) and most people (inaudible).

Q9: What gives you (inaudible 37:14) if you take what do you think you have to do (inaudible) six or 12 or 13? Is there anything to make you more...

Sheila Tighe, NP: Pardon?

?: We couldn't hear that question.

Sheila Tighe, NP: Dr. Griffiths, do you just want to come up here a second. He's just asking what can you take for the get up and go? Ritalin. No.

Elizabeth A. Griffiths, MD: So, everybody is an individual and everybody's symptoms are going to be different. I think some people are fatigued because of the fact of the cancer itself. Some people are fatigued directly because of anemia. Some people are fatigued because of depression. I think there's a wide variety of symptoms that present as fatigue or wide variety of causes of fatigue and individually I think there is no panacea for all. So, for some people increased transfusion supplementation may make people better. For some people pushing to make the hemoglobin better might make them feel better. For other people an exercise program. One thing that I would say again not to tout exercise as the be all and all, but for any degree of anemia your physical reserve to tolerate that degree of anemia depends on your level of activity. So, the less active you are and the less used to the level of hemoglobin that you have the more likely you are to be fatigued and so I think it is really important to maintain functional activity and that means walking. I mean, I don't expect everybody to get on the treadmill and run six miles, but I do ask my patients to go for a walk on a regular basis and when I say that I mean 30 minutes of walking if you can, three days a week or more because if you can do that you can push yourself you actually improve your physical reserve and

you'll tolerate whatever degree of anemia you have to a much better extent. I also think that by exercising and moving people feel better. Humanity was not intended evolutionarily we were supposed to be out walking around all day. We're not supposed to be sitting around facing our computers and watching television. So, I think all of us do better if we move.

Q10: The energy (inaudible 39:28)

Elizabeth A. Griffiths, MD: So, those are high dose caffeine and high dose B vitamins. I personally would not recommend them. I see a lot of people who do those and who show up to my clinic with atrial fibrillation from too much caffeine. When I say a lot I've had at least two people do that. So, that puts me off a little bit. Also if I take too much caffeine it always makes me feel unwell. So, that's not my recommendation.

Q11: Can exercise actually raise your red blood count (inaudible 40:00).

Elizabeth A. Griffiths, MD: Yeah. Certainly and again, 30 minutes is the be all and end all. I would recommend people go for as much of a walk they can tolerate and just the fact of moving will make you feel better. Does exercise raise your hemoglobin? I don't think so necessarily, but I do... I mean, there are some data in mice that have an MDS-like syndrome that by exercising you can mobilize some of your stem cells from the blood and that by doing that the ones that are less fit get killed off although that has not been proven and the repeat experiments that my colleague who did some experiments to try and recapitulate that mouse data was not able to prove that it was true. There's in theory some theoretical ideas about that, but what exercise will do is it will train your system, your heart, your lungs, everything about you, your muscles to function better for the degree of hemoglobin. So, I can give you a personal example. My little sister for all of her life decided that she wanted to be vegetarian. She started this at the age of six and she was a vegetarian for all that time and she does not like to eat eggs and she doesn't like to take her vitamins and so one day she called me and she said, "Elizabeth..." My sister is a long distance runner. I should preface this by saying that she runs marathons on a regular basis. She called me and she said, "I'm still worried. I can't run for more than two minutes," and so we sent her into the emergency room and her hemoglobin was five and it turned out that she had a very profound iron deficiency, but she was living on the third floor walkup in Rome and she was walking all day every day with her hemoglobin of five grams and they said to her oh, my God. How can you possibly do this? But she was running and walking still four or five miles every day with a hemoglobin of five grams and I think the point here is that she was very well compensated for her degree of anemia and she was very physically well and so depending on how fit you are and how used to your level of anemia you are you can tolerate much more and so it's a point of fitness and so if you maintain your fitness if you keep walking and keep pushing yourself your body will get used to the lower hemoglobin and you'll feel better even if we don't change your hemoglobin and so to the extent that it's possible and, again, I don't expect you to get up on... I don't want you to come with spinning class with me every morning. You don't have to spin for 40 minutes and push your heart rate as high as it will go but a little bit will make you feel better. In my opinion that's just common sense.

Sheila Tighe, NP: Sure. Just keep Dr. Griffiths...

Q12: I have a question. Quick question. In the State of New York my oncologist will give me Procrit if my hemoglobin is 10. In the State of Florida, the oncologist will give me Procrit if it's 11.5 and below. Why is there a difference like that?

Elizabeth A. Griffiths, MD: So, the package insert for management of hemoglobin using Procrit or erythropoietin stimulating agents in cancer in general does not allow you to give it for say, for example if you have cancer and you're getting Procrit if your hemoglobin is above 10 for regular cancer. If you look at the package insert specifically around the diagnosis of myelodysplasia it's acceptable to give for a hemoglobin below... anything below 11 and that is because in solid tumors, in the solid tumor literature and in patients with renal failure who also get treated with that drug they have seen an increase risk of cardiovascular death if you push the hemoglobin above 10 and so if you have other cancers and your doctor is an oncologist who treats mostly other solid tumors they probably are uncomfortable pushing your hemoglobin above 10 whereas maybe your doctor in Florida is more a hematologist and is more treatment patients with MDS. So, that's probably the distinction and it's based on the risk of heart attacks and strokes and clots that can happen in patients with kidney dysfunction, people who are on dialysis who get Procrit because I told... remember I told you that EPO is made in the kidney. It's a copy of the kidney hormone. So, people who have end stage renal disease who are on dialysis they often need supplementation and solid tumors where the risk of blood clots is often higher intrinsically because the cancers secrete hormones that increase clotting.

Sheila Tighe, NP: Yes?

Q13: (Attendee) here was diagnosed about 18 months ago with MDS as a result of just some routine blood work. I'd be curious if anyone would share how long you've been living with MDS. Here's a year and a half, but do we have like 10 years, (inaudible 45:23)?

Q14: (inaudible)

Q15: Three and a half.

Q16: Four.

Q17: Seven.

Q18: (inaudible 45:34)

Q13: Thank you.

Q19: So, my question is there a difference between duration in MDS compared to a CMML?

Sheila Tighe, NP: Did you hear that Dr. Griffiths?

Elizabeth A. Griffiths, MD: So, we don't have as much data for CMML just because it's a smaller patient population. Patients with CMML-1 that's to say a lower blast percentage seem to live longer

than patients with CMML-2. There are some mutations with CMML that are associated with a higher risk of progression we think. Many people especially if a patient is very young we all worry about CMML being a potentially a worse actor than low grade MDS and so many physicians would keep a close eye on somebody CMML to make sure that they're not developing CMML-2 or accelerating because some of the mutations associated with CMML are associated with a more proliferative phenotype. Does that answer your question?

Q20: I was diagnosed 2 ½ years ago only through a routine blood test with a new doctor because I was real tired. So, I was wondering if there was a percentage of people like the gentleman up there and myself were diagnosed just like if they had no symptoms.

Elizabeth A. Griffiths, MD: It's a pretty big one. Especially based on the awareness (inaudible 47:25)

Q21: Is there a big difference between men and women as far as are affected by this?

Elizabeth A. Griffiths, MD: There is a male predominate in terms of making the diagnosis of MDS. (Inaudible 48:00). We actually don't know why that it is. (inaudible) because men are exposed to (inaudible). People who smoke (inaudible)

Q22: So, their history is (inaudible 48:46)

Elizabeth A. Griffiths, MD: We don't know. We've observed (inaudible 48:49) that more men (inaudible).

Q23: I have a question about dietary. So, you had mentioned a neutropenic diet. I was just wondering how often to do that? (Inaudible 49:18)

Sheila Tighe, NP: When someone's neutrophil falls below 0.5, we institute a neutropenic diet. Dr. Griffiths is not as stringent with her patients, but we definitely say like avoid berries. Those things can have fungus on them. Fresh fruit. Someone should be washing the fruit, peeling it for you. Stay away from salad bars. You don't know how long that food sits out. Avoid cold cuts just because they can have bacteria. Cooking things is always better than leftovers. Things like that.

Elizabeth A. Griffiths, MD: Can I just make a comment here? So, the data for neutropenic diets are derived. They come... the idea that this a bad thing to eat fresh fruits and vegs and all that stuff comes from early data in patients getting bone marrow transplant and patients getting chemotherapy, high dose chemotherapy. For patients with MDS the risk is probably less and it is my view that eliminating all salad from your diet is very unpleasant. So, it is my recommendation to my patients and, again, the practice varies quite widely. I know that there's some people here from out of town and I don't know if Hopkins is doing this. When I was a fellow at Hopkins... I trained extensively. I was at Hopkins for eight years. We did not institute a neutropenic diet, but we did say we don't want people to wash their fruits and vegs and we want them to peel things and what I say to my patients is berries very frequently have mold growing on the exterior. So, if you leave your berries... if you look at your berries and even if you get it fresh from the grocery store. If you open that up there's often

mold in there and the number one problem for my patients who are neutropenic especially patients with MDS who were neutropenic for a long time is the development of mold infections in the lung. Now, we live in a soup of mold. Mold is in everything. It's in the soil. It's on all the fruits and veg and everything and molds live with us and most of them are fine, but if your immune system's compromised you may grow mold just like the bread that you leave on the counter can grow mold and mold is an organism that's a little bit more complicated than bacteria and it's a little bit more like us as human beings in terms of its genetic complement and behavior and so it's a bit more challenging to treat and so the antibiotic and antifungals that we use prophylactically tend to be a little less well tolerated, tend to be a little bit less pleasant to take. The usual prophylactics that we use for people who have prolonged periods of neutropenia are one of the azole antifungals. The three medications that are in this family are Voriconazole, Posaconazole and Isavuconazole and for patients who are profoundly neutropenic for a long periods of time we often will use those as preventive, but again I don't think it's reasonable to ask people to stop eating salad for the next 10 years of their life if all goes well. So, I just say wash it, be thoughtful. If it's rotten don't eat it. Don't eat on salad bars and try to avoid old cold cuts that have been sitting around for a long time. Fair enough? Again, common sense.

Q24: My hemoglobin count started dropping very, very gradually a number of years ago. I'm saying like 10 or 12 years ago and I was on Methotrexate and I was taken off of Methotrexate, but it still continues to just drop very, very slowly and I wonder I don't think correct me if I'm wrong, I don't think MDS is you get it overnight. I think it was a very gradual process. So, to say when I... I guess I've been starting to go to smarter and smarter doctors because now I'm diagnosed with MDS, but I think maybe I have the beginning of it that many years ago because after, I mean, I've been off of Methotrexate for now probably 10 years at least and it still just continues to drop very, very slowly and so it's not an overnight process. Is it? It's just... so to say I've had it for four years, I've had the diagnosis for four years, but I have no clue how long I actually have had it and how far I am in the process.

Elizabeth A. Griffiths, MD: I think that's extraordinary (inaudible 54:23). That's exactly my feeling about this disease. So, when I describe it people who've seen me in clinic I sometimes tell them people ask me is this leukemia? What is this? And I say this is kind of a cockroach problem. It's probably there. It's probably been there for a long time. It slowly accumulates over time. That's why I said when you start to see the bone marrow blasts increasing when the blasts increase over time usually with this disease at some point if you live long enough maybe it would increase and you would get to above 20 percent and then we would call it AML, but I would argue that there's a distinct clinical entity of acute myeloid leukemia that presents today that was not present a month ago, two months ago, three months ago and that is a distinct thing from people who have mildly low blood counts for a long time why then develop more profound blood counts, more profound low blood counts and then have an increased blast percentage in the marrow, maybe 19, maybe 20 percent. That's, I think, a different disease. I think that's a different disease entity and we need to think about it differently because if you have an MDS associated AML and you had an MDS diagnosis six months ago or a year ago and all of a sudden now you have 20 percent blasts the pathophysiology of that process, the underlying mutational spectrum, the underlying behavior of the disease is in my view is quite distinct from somebody who had nothing six months ago and now has acute leukemia even though when you look under the microscope the absolute blast percentage for

those two people might be the same. Does that make sense to everyone? So, if I have a cockroach kind of disease it might not be the case but high dose chemotherapy which is designed essentially like napalm to kill everything that's growing quickly might not be quite as effective and that's indeed what we see in patients with MDS or AML out of an MDS diagnosis who get napalm like chemotherapy. Now, all the chemo that we give, the high dose chemotherapies that we give, those are all DNA toxins and they capitalize on the difference in terms of turnover time between the cancer and the normal. Does that make sense? So, Cytarabine and Daunorubicin what they do is they poison DNA replication. They poison the ability of your cells in your body to copy mother to daughter strand of DNA. Does that make sense to everyone? So, they poison the ability to copy your chromosomes. If the disease you have is a relatively slower growing disease that took a year to go from a blast percentage of 10 percent to a blast percentage of 20 percent the approach with high dose chemo might not be as effective as it would be for someone who went from nothing a month ago to 80 percent blasts today. Does that make sense? So, it is my view that our thinking about the distinction between MDS and AML has to evolve from thinking about it as a disease that is defined by the blast percentage today to defining it based on the mutational profile and, indeed, what we find is that specifically patients respond differently to chemotherapy based on their mutational profile. To see mutations that are similar to the MDS background, those people respond less well to aggressive chemotherapy regimens and better to drugs like Vidaza or Azacitidine and Decitabine and maybe to different thinking. Different approaches and so I think from my perspective it's important to understand conceptually that these are two distinct entities and they have distinct clinical outcomes and distinct of responses to therapy and so I always tell people from my perspective MDS is a cockroach. It's hanging out in there. It's not dividing too quickly. It's really a pain. It's probably been there for many years and so thinking that you're going to be able to wipe it out by taking a quick shot or just burning everything is not a logical approach.

Q25: So, if you have... if you're anemic for many years, but if you have a (inaudible 58:46) is normal then a couple years later it's not normal would you think that MDS all the way through even before it showed in the bone marrow or how would you actualize that?

Elizabeth A. Griffiths, MD: So, I think it's a little bit like asking a question about when you took the picture in time. So, if I do a bone marrow today and you don't have dysplasia but you're a little bit anemic and I look and I find a mutation and that mutation represents 15 or 10 percent of the total cells in there that mutated cell may be secreting some hormone that's impeding the normal production of cells. We don't know for sure but we think maybe that's what's going on and then I do another bone marrow in two years or four years and now I see some dysplasia and if I look at the allelic ratio maybe that allelic ratio is now 20 or 30 percent I think it's a little bit like gerrymandering election like in voting. So, where do you want to put that line? If we take that all the way to the end you could imagine... Have you guys all seen the film "Gattaca?" You remember this old movie, dystopian future now many years ago. Too old. You guys were not watching the movie. So, in that movie the idea is that we are molecularly profiling everybody's genome at the time that they're born and we are treating them for their future history of heart disease when they get born and so we start treating them before and then the end point of that is engineered kids where we weed out all of these potential risks for developing problems. Now, we're not there, but I think that question is a little bit like what you're saying. If you have a problem that might present itself in the future I don't want start treating you today unless I have a treatment that's going to change the natural history of

what you have and it doesn't really matter if I call it today or tomorrow. We call that ascertainment bias in the field. We say we found it earlier, but it can change the survival. So, it looks like you're living longer when I find it earlier. It looks like you're living longer, but I just didn't find it until later and then you're living a shorter time, but that doesn't change the natural history. Does that make sense to everybody? Okay. And so I think that's a little bit what we're talking about here. We can call it MDS earlier. It makes us all worry because then we get online and we read about MDS and we see that the outcome for MDS patients mean in survival for high risk MDS is six months. So, if we do that we scare ourselves then we spend a lot of time being worried and then the quality of our life which is what all of this is all about is impeded and is not good. So, I think it's important to take all of this with a bit of a grain of salt. Every single one of us all we've got is today. You wake up in the morning, have your coffee in the morning and do your crossword puzzle with the people you love. That is what life is about and we could all get killed off by nuclear holocaust tomorrow or the sun could explode, but unless we enjoy today there's no point and that's true for every single one of us and so I think it's very, very important to kind of think about the disease and think about outcomes and make plans but also to live every day and this is my personal philosophy. I'm bending all your ears.

Q26: I think my lab reports said that I have Trisomy 8. Is that correct? Would that be the correct term? Trisomy 8?

Elizabeth A. Griffiths, MD: (inaudible 1:02:37)

Q26: And it's also fairly common with MDS.

Elizabeth A. Griffiths, MD: Yes, that's correct.

Q26: Is there anything that makes it worse or does it not matter? Is it a kind of mutation that it'd be better not to have it?

Elizabeth A. Griffiths, MD: So do you remember when I presented the slides using the cytogenetic profiles from more than 2,000 patients with MDS who received no disease modifying therapy they were able to make predictions about survival based on the presence or absence of cytogenetic abnormalities. Do you guys remember that slide? So, I cannot speak to individuals. Trisomy 8 is a frequently... many of these mutations are frequently identified, relatively frequently identified, in patients with MDS. So, we know that Trisomy 8 occurs in AML and MDS. It's considered an intermediate risk cytogenetic risk classification. Many of the cytogenetic risk classifications are considered intermediate. That means we don't really know. Sometimes it's associated with indolent outcomes, sometimes it's associated with more aggressive outcomes. For individual people who have individual problems then... individual experiences of their MDS each person is distinct. I don't know if that answered your question.

Sheila Tighe, NP: I'm not sure if we have any other questions, but I think we will be moving on shortly to the next presentation. Is there anybody else that has anything they'd like to ask or share before we turn things over?



Q27: (inaudible 1:04:26)

Sheila Tighe, NP: Yes, is on iron overload, I believe. This is the end of this...

MDS Foundation: It's at two o'clock. (Inaudible 1:04:37)

Sheila Tighe, NP: Just a minute please. We've got someone that would like to say something.

Q28: Before I came today I only knew one other person who had MDS and you've been so helpful (inaudible 1:04:58) in Buffalo and people (inaudible).

Sheila Tighe, NP: I believe and I'm stepping in for my colleagues from the US. I'm from Canada and I do what they do in Canada, but I do know that they have support groups. So, I'm thinking if there's a way that you wanted to get it started would be to contact the MDS Foundation. You could probably contact Audrey and they may help you facilitate that because as you say I think so much of the battle is spending a day like this talking to other people. The question up here from the gentleman that was just diagnosed 18 months ago to see somebody five years later who is still doing well. I encourage all of you to reach out that way and if not in person there's a lot of online support and I know the MDS Foundation do a wonderful job of connecting people. So, really encourage you to do that.

MDS Foundation: So, the next portion is a talk on iron overload that's sponsored by Novartis. It's not officially part of the... (END OF AUDIO)