Speakers:
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Kelley Anderson, RN: If everybody's finished eating for the most part it looks like I'm going to jump in and just get started. You can work on your surveys just like with other presenters please feel free to ask questions. Myself and Dr. Klimek will answer them to the best of our ability and I do want to leave time at the end for like open discussion and questions. So, there'll be plenty of time at the end also.

So, first of all I want to thank everybody from the MDS Foundation for the delicious lunch. That was great. I'm ready for a nap. So, hopefully I'll try to be engaging enough to keep everybody awake for the next hour or so.

So, I'm just going to do a brief review of kind of what was discussed this morning. A good question that a lot of our new patients have is when do we start treatment? There are a lot of things we take into consideration when we decide if it's appropriate for you to start treatment for your MDS. Increasing transfusion dependence, progressive or symptomatic cytopenias which is low blood counts, if you're having gum bleeding, if your platelets are really low, if you're starting to have infections because of your neutropenia or you're really suffering with your anemia, rising blast count is a big one or if you have high risk disease we're a lot more likely to jump into treatment more quickly, but treatment is we try to be as individual as is possible. We want to work with you, with your family, with what's important to you and your life and we also look at your performance status, fit versus frail. Are you in good shape for your age, do you have a lot of comorbidities, is it going to really knock you out if we give you a round of chemotherapy? It's something we try to… we don't enter treatment lightly. So, we really want to talk to you and your families about what your goals are in your as we move forward in your life. If you have any comorbidities. Your risk category which Dr. Klimek covered earlier, the lifestyle you like to lead if it's more important for you to be able to go golfing, go on trips and you would prefer to get supportive care versus coming in and spending a lot of time getting therapy and personal choice really we like to call Dr. Klimek the caption of the ship, but it's you. We're just there to give you navigational support and to give you our best opinion, but really you are the one who's in charge of your treatment decision.

So, as Dr. Klimek mentioned bone marrow transplant is the only cure for MDS, but it's not an option for many of our patients because of their age, because of other illnesses or there just may not be a suitable donor available. Age alone does not exclude people from active therapies. We have plenty patients that are well into their 80s and 90s that do fantastic on treatment. So, just because we never would look at a number on a piece of paper and say that we wouldn't treat you. We want to look at you and your whole… you as a person and what we call your performance

status which is we look at your comorbidities, your activity level, your counts and your support system.

The one thing that patience is a virtue and all of our therapies take time to work and the next couple slides I have are going to discuss the timeframe that it takes for MDS therapies to start working. Generally, it's four to six months of continuous treatment before we would say that this treatment is not working for you and you know what? Your counts are going to get worse before they get better. If you're already struggling with anemia, you're already getting transfusions you're probably going to need more, you're probably going to be more fatigued before they start getting better. So, we really want to proactively manage the side effects early on in treatments that we can know what to expect, give you and your family expectations and kind of plan ahead.

So, this is the like Lucy chocolate factory that Dr. Klimek talked about. This is your bone marrow. As your counts are starting to drop before you start treatment all of the good cells are getting crowded out by the cells that's hyperplastic state. There's just not enough room for your body to make good working platelets and good working white blood cells and good working red blood cells. So, then we start treatment and the treatment is going to clean out the bone marrow, but you're going to see your counts drop further. This graph over here is of neutrophils and as you can see it drops off about six weeks into treatment. Your counts are going to get lower than they are before you start treatment which is why we give you supportive medication like antibiotics, antivirals and antifungal medications and you'll likely need more blood transfusions. Say you are getting blood transfusions every two weeks. They could become weekly. That is something to kind of plan for. It's something you should discuss with your physician and this is the great part that we start to look forward to about four to six months on in we hope to start seeing a response to treatment. We hope to start seeing when your counts recover that 21 day mark that Amber talked about about three weeks after you get your chemo we hope to start seeing your hemoglobin recover more, your white count recover more and your platelets recover more and as time goes on that's going to help mediate your symptoms of MDS. So, you're going to be less anemic on your own without transfusions and then as time goes on our goal is to have you need less supportive care. So, need less platelet transfusions, need less red blood cells transfusions, maybe even not need the (inaudible 5:31) all the medications that we give you that maybe you don't have to take 12 pills a day for us anymore, but the real challenging part and the part that we want as healthcare providers for you to talk to us about is this part here because you're going to feel worse before you feel belter and I know that it's really challenging sometimes, but we're working towards here and everything looks great. So, don't get discouraged. This happens to everybody. A lot of people see their counts drop and they think their disease is getting worse, but that's not the case. It's the therapies we're giving you are going to cause that to happen.

So, just to review really quickly it's going to take a minimum of four to six months before we would tell you your therapies aren't working. We're going to expect your blood counts to get worse before they get better and to get through the first cycles of therapy really just I as a nurse I

answer the phones for Dr. Klimek. I would rather that you call me about something than not call me. Like please I love talking to you on the phone. That's my whole whole job. Dr. Klimek, we're all around. We're here for you. Please never hesitate to reach out to either us or your normal physician. Don't be disappointed if we modify your dose or we delay your treatment because we think that your toxicities are too bad. Your counts are dropping too much we may decrease you to five days of Vidaza instead of seven. Again, we strive to provide the most individualized care possible and sometimes that involves decreasing the dose of medication that you're receiving.

And this is a graph that kind of shows us… so, the purple is our hemoglobin, yellow is the platelets and the blue is the white blood cells. This is the beginning of before treatment. First cycle all the way through four cycles. This is a patient that's moving toward bone marrow transplant follow up, I believe, but as you can see the counts are getting worse through cycles one and two but then as they start… then they start to recover by the end of cycle four hemoglobin, platelets and white blood cells have all kind of gone up to almost a near normal range.

And then this is a patient over 10 years of getting Revlimid charting all of their counts. Your hemoglobin is never going to be what it was before you started treatment. It's very unlikely you'll be 13, 14, 15 again, but typically patients are asymptomatic when they're around 10 or 11 and that's our goal is to get you to a livable, workable new normal. So, this is a patient from 2002 to 2011 on Revlimid. Just very… these counts are very stable. We would be very happy with this.

Now, we get to my favorite part which is talking about partnering with your care team. My favorite word as a nurse is advocate. I come to work every day thinking about how I can be the best advocate I can be for my patients, but it's important that you advocate for yourself, too. Coming to things like this and becoming informed about your disease there's nothing better that you can do.

So, here is some tools and strategies for success. All of this is also outlined in the books that the MDS Foundation gave you earlier today and we'll discuss at the end the *Building Blocks of Hope* is also a mobile app now which is very great and all this information is accessible through there as well.

So, we're going to talk about how to get the most out of your treatment, about becoming a partner, about our caregivers and how we can support them while they support us, asking for help, staying well and building a plan.

So, how do you get the most out of your treatment? Like I said it's important to understand your disease. You should know your risk category, know what your normal blood counts are and track them. Ask for copies of your lab results. We're always happy to give them to you and you can

have good perspective of what your disease is doing. Hopefully as good a perspective as what your health provider has. It's important to take your medications as prescribed especially the medications we give you if you're neutropenic. I know that besides from taking acyclovir and taking antibiotics all the time isn't fun. They can have some side effects, but it's really very important. Please keep your appointments and your visits for treatments even when you're doing well because the only way we know your disease is changing is by watching your counts. Ask your provider about symptoms that need to be reported immediately. Things like fever and bleeding, shortness of breath. Use common sense about calling 911 if you're having chest pain. We can always get you to the hospital if you want to… if you need to go to a local ER we can always get you to MSK or to your main center. It's most important that you're evaluated by a provider. Keep track of your symptoms that way you can tell us if things are getting worse or things are getting better and that's how we know things are working. Talk to your provider candidly about goals and the expected duration of treatment and what's important to you and always don't hesitate to reach out about financial assistance programs especially the drug companies have a lot of money that they can help out. Sometimes they have stock of drugs that you can get drugs for free. Amber's an expert with that. I'm lucky enough that I can just send her cases and she makes phone calls and people get assistance, but they're really are an infinite number of resources out there and we're happy to point you in that direction. So, shared decision making is one of my points of passion. I want to know what you want to do and how you want to treat your illness. We can tell you what based on your numbers and based on studies what things look like, but it's important for us to know what is important to you.

So, how can you have the best office visit with us possible especially if you're coming into like New York City to see your physician? We want to make sure that you have… you make the most of things. So, set an agenda. Sit down with your family members especially those that are involved in your care – daughters, grandchildren, partners and ask them what you want to get out of your visit if they have questions that they want answered. Prioritize. Maybe pick the top three things that you want to discuss just because sometimes conversations can go long and you don't want to miss out on your most important item. By focusing on this agenda you can make the most of your time. I know it's fun and I love hearing about everybody's activities and grandchildren and all that stuff, but if you have important questions you needed answered please interrupt when I'm chatting about social things and tell me about the questions you have. Preparing questions before the visit. As much as I'm happy to answer your questions on the phone when you call after a visit, it's best when we have the whole team present and your family present if we can discuss questions together. Start with that list. I recommend keeping the list and keeping your list of answers and I really… it's best if you can have a member of your support team present that can take notes during the visit so that you can be engaged with your physician and not worried about writing everything down. Please make sure that your physician has an up to date list of your providers, anything that's changed if your blood pressure meds are different if you've had a weird rash, your vision, anything. We want to know all the little details. Keeping a symptom log is very important. The app that we're going to talk about at the end has the ability to track your symptoms which is really very helpful because it just could be right on your phone

and any test results that you saw your cardiologist and had an echo make sure you bring that information with you and then, of course, transfusion records. If you follow with multiple physicians and one is managing your transfusions we want to make sure that everybody has that information.

And make sure that when you leave your visit you have a clear understanding of the plan. We don't want you leaving more confused than when you came in. I know oftentimes we give you an overwhelming amount of information, but we're always happy to take the spare three minutes at the end of the visit to make sure that we're all on the same page moving forward. Know when your follow up appointments are. Know any instructions for new or existing medications if they've changed. If there are other providers that we want you to see and then again, things that you should be reporting like fevers. Make sure that you're aware of when to call who and how to get around the office, who you talk to for what problem.

Where would we be without our caregivers? Our partners in care. Everybody, the whole family is affected by an illness. So, we try to really urge caregivers to take care of themselves, maintain a healthy lifestyle and make sure you're eating, exercising, sleeping as much as you can. If you have a spiritual community that you remain engaged that you guys still manage to do things that you find fun and bring you joy in your life. That's the whole point of why we're extending your life with life extending treatment is so that you can enjoy it. So, I think it's very important to strike a balance and asking for help, I know it's not always easy to tell people that you have needs and especially if you're not the ill partner. Sometimes it's hard to say that I need a break, but there are so many people in your life that want to help, so don't be afraid to ask.

This is a great website about building and organizing a support team. It's called Lots of Helping Hands and I'll show you on the next page because it has… it kind of shows you the calendar. So, it's website, one person or several of you can sign in and it's a free… you coordinate a calendar. It's very quick, but you can organize when a patient needs meals delivered, if they need rides, if they have various appointments and friends and family members can check in and they can see what days maybe on Tuesday the patient needs a ride to chemotherapy. So, people can volunteer to help because everyone's going to always ask how can I help? What do you need? This is a great way that you don't have to keep track of everything as much. People can jump in themselves and reach and out and volunteer and it sends E-mail reminders also so it reminds… they don't forget to drive you to your appointment.

Q1: (inaudible 16:31)

Kelley Anderson, RN: Yes. It's amazing how people… People want to help. (inaudible 16:53) people that care about you want to reach out and people often just don't know and people are nervous to ask. They're nervous to ask how things are going and you have so many digital tools now I think it's really important to try to take advantage of them.

I recommend every day even on hard days of treatment to take a moment and think about the things that you love to do, what you can still enjoy and what you want to work toward enjoying again. There are things that you can do to get to that point like with eating a balanced diet, quitting smoking, limiting your alcohol intake. Try to be active every day even when it hurts even when you don't want to. The more active you are, the more you push yourself the better you'll be able to sustain a) tolerate your treatment and then you'll be able to do more and more. Fatigue feeds fatigue. It's just by sitting on the couch when you feel bad you're only going to feel worse, but also get enough rest and as you move forward with your provider you'll learn what are symptoms that they need to know about, what are symptoms that I can talk to them about the next visit, but like I said please always call with something new, something weird. We want to know about it.

As I said, exercise is the single most important way to combat fatigue. Use it or lose it is very, very real. If you don't stay active you're going to lose it and it can happen very quickly, too. It can happen… if anyone has to raise your hand, but if anyone here had a prolonged hospital stay getting out even after just a week of being mostly in bed it can take months to get back to baseline. We really want you to try to push yourselves as much as you can. Strength training, things with bands or light weights, physical therapists love, love, love to show you ways to work with what you got. It's their favorite thing. They're all like little MacGyver's. They'll come up with ways of like… they're really fantastic. They showed me things that just blew my mind. So, you can ask your provider for a physical therapy consult even if it's someone coming to your home and working with you. If you're more active a lot of the centers offer group yoga classes and so it's not just going to your gym because gyms do have a lot of germs and that can be concerning, but you can come to the center and take classes. Even just going for a walk around the block especially while this weather's… well, not that it's nice today, but while the weather's nice out or taking the dog for a walk. Other ways to help with your fatigue is try to not eat too close to bed. Don't take the iPad or iPhone to bed with you. The blue light… I know, everyone's looking at their (inaudible 19:46) with them. I'm guilty of it, too. The blue light is really detrimental which is the light that comes out of electronic devices. It's really bad for circadian rhythm. So, bring a book. Try to keep your sleeping spaces dark, quiet, comfortable and do whatever you can to help your body relax. If you're having trouble sleeping please tell us. We don't know if you don't tell us and we have lots of recommendations.

Nutrition. Stay hydrated. No one here probably drinks enough water. I don't drink enough water. I know that it can be challenging because it got eight bottles to eight glasses of water sounds like you're going to be running to and from the bathroom all the time. Really, it's the best thing that you can do for yourself. Don't drink it too close to bed that you're waking up in the middle of the night, but especially if you're on treatment staying hydrated is still very important particularly the anti-nausea medications that you sometimes receive with chemotherapy are extremely constipating and the best way to stay ahead of that is to stay hydrated and just staying moving. Most physicians' offices including Sloan Kettering have great nutritionists that'll sit down and talk to you or on the phone for a half an hour or an hour about your personal

nutritional needs and give you a diet plan. There's also a tremendous amount of information available online on MDS Foundation has some information, cancer centers. Limit or exclude alcohol intake. Make sure you're getting enough calories. Make sure they're good calories not empty calories. Now is not the time to jump into the newest fad diet of eating only grapefruit for 21 days or whatever is on the talk shows this week, but… and before you start a supplement as Amber said always talk to us about it and then food restrictions really are based on your counts if you're very neutropenic there's a long list of limitations of foods that we want you to avoid.

Avoiding infection. Luckily we're out of flu season, but there have been some pretty gnarly colds and viral things going around. So, especially when you're on treatment we're going to be monitoring your blood counts weekly. If you're not on treatment that's up to you and your physician how frequently we want to get a record of what your counts are doing. Try to avoid people who are obviously ill. This includes small children and if you are around small children wash your hands often, wash your hands often anyway. I keep Purell all in my purse. I recommend just a little travel bottle. As far as symptoms that need attention, call your doctor if you even… even if you just think oh, it's just a sinus infection. It's just a cold. We want to know about it. We consider a fever 100.4, 100.4, which is lower than you probably grew up thinking what a fever was, but when you have neutropenia that's what your fever is now. Avoid taking Tylenol around the clock because you could be having fevers and not even knowing it. The same thing with Ibuprofen. Talk to your provider about medications that can inhibit your fevers. Get your flu shot every year. That goes for everybody not just neutropenic and make sure people in your family are getting vaccinated as well. The pneumonia vaccine you can talk to your PCP about. We do not recommend the shingles vaccine for patients that are immunocompromised. So, we want you to talk to us before getting any vaccines.

Q2: (inaudible 23:37)

Kelley Anderson, RN: Yeah, I believe that's the recommendation. We don't want you (inaudible 23:50) like you can bring into the house. If you're immunocompromised so you're not often on antivirals, but that's not… we'd rather you not be exposed to it at all.

And I know there's been a lot of questions about platelets today. So, once your platelet count is below 50,000, you're at an increased risk of bleeding. Staying ahead of constipation is really important. Oftentimes I recommend patients adding something like Senokot along with a (inaudible 24:23) and hydration to make sure that they're not having constipation because that can cause rectal bleeding and tearing especially when your platelet counts are that low. Be careful about blowing your nose. Don't pick your nose. Use a soft toothbrush and there are still other recommendations but those are kind of the biggies that jump to mind. We're going to monitor to your blood counts weekly so that first eight weeks of treatment and then clinically as indicated we're going to see how your counts are doing, how things are looking and then make a decision from there. We don't make you come in more often than we need you to. I promise. It's not… We try to work around your life as best as possible. Avoid aspirin, aspirin containing

medications and Ibuprofen. If you are on a blood thinner because you have a history of atrial fib or a blood clot that's something to talk about with us as well as your primary care physician as your platelet counts are dropping because that's something we'll play around with. Even if you're seeing us every week please still stay in contact with your primary provider and any specialists that you have – cardiologists, neurologists, endocrinologists. They're specialized in their field as we are in oncology. So, we really still need them to be a part of your care and if you come down with something small and viral you can generally pop into your physician's office instead of having to go into the emergency room or come into the City. Oftentimes it's hard to get into your specialist's office same day. So, it's important to keep that relationship with your primary care provider and keep us up to date as well as to what provider's you're seeing. Make sure we have their contact information so we can send them any notes and lab work.

Palliative and supportive care for cancer is something that's close to my heart and Dr. Klimek's heart. We work very closely with the palliative care team at Memorial Sloan Kettering. We actually have a nurse practitioner that's implanted in our clinic. When new patients that are newly diagnosed with MDS are coming to our clinic we're rolling out a program we call it One Two Three Project. That's about assessing symptoms including distress and psycho-social issues every single visit so that we can address issues before they become issues. I know that when a lot of people hear the word palliative care they thin hospice and that's just so very much what palliative care is anymore. There are teams whose whole focus is on your wellbeing be it physical symptom management, emotional management. They're really just fantastic. I can't speak highly enough of them and they work with us not two separate teams. We all meet and discuss everybody together. So, that's our combined terminology palliative and supportive care depending on the institution you're at. They're generally kind of interchangeable.

So, in the *Building Blocks of Hope* book under tab five it's the MDS plan and it's where you can go to help you understand about your diagnosis and help you build your individualized treatment plan and there's several tools that are in there. We recommend that you make extra copies that if your family members want more copies or as you fill up pages so you don't need a whole new book. This is very, very exciting. I've only recently started fooling around with it on my phone an if anybody wants to download it today we can download it today. I might be opening a can of worms, but the My MDS Manager app, it's from the MDS Foundation. It's fantastic. There's actually a great little YouTube video on the website that runs through all of 6 1/2 minute long runs through all of the things that are on it, but you create an MDS profile where your score is in your bone marrow results, your profile. You can enter your labs and track them. Track when you get transfusions and treatment. You can list all of your professional and personal contacts. It has a symptom tracker. You can have track your medications and you can set reminders. So, as your reminder to take your medication. You can upload reports directly into the app and it will sync with your calendar and your phone. There's also the virtual support network which it takes… I have a Gmail account which is what I use, so I didn't run into that, but I guess… Google accounts you can save your data and use it on multiple devices. It will group… you can reach out to people with the same risk category or comorbidity score and it lists available clinical trials and

it's supported by the MDS Foundation who are fantastic, but this is very exciting and there's more… it's newly rolled out and I'm sure that there's going to be more features as time goes on.

Alright. We're up and running.

Q3: (inaudible 29:41) it might have like a download as download (inaudible)

Kelley Anderson, RN: See. Everybody's ahead of the game. You guys don't need me.

So, this is just the information about the manager. You go into the app store on your phone and MDS Manager and you can download it right from there. Yeah. This is just the… I'm sorry this slide's so small. This is just a list of all the people that (inaudible 30:21) and then a list (inaudible) search describe MDS Manager (inaudible).

It's very easy to find. It's really… I sent it to all the nurses in my practice and everyone was really excited. It's really… and it sounds like there's more in the pipeline, too, that… but these are things that are great because if we're seeing you every month you may forget that a week after you saw us that you were feeling so fatigued that you didn't think you were going to be able to get off the couch that day and then you see us and you talk to us and we have a great conversation, but by doing something like tracking your fatigue every day and having a number and then you can show us. You can bring it in and say this is kind of how I felt over the last month. That is a tool that is such a gift for healthcare providers to be able to see what you were feeling. We can't see it real time, but we can look back with you and then ask you better questions.

The MDS Foundation also has a patient outreach and advocacy program. This is the contact information for the patient liaison, Audrey. I think Dr. Klimek has a little bit more to discuss. Yeah. Do you want to do some questions (inaudible 31:53)?

Q4: (inaudible 32:06)

Pretty much just about everything. So, your body is amazing machine that sees all of these white blood cells that are fighting things constantly. Viruses, fungal infections, bacterial infections. You cut your finger and you don't think twice about it. You may put some Neosporin on it, but when you don't have an immune system to fight it off those things can become life threatening. Some things as simple as urinary tract infections you end up very, very ill. So, we just try to… and there are some infections like fungal lung infections that you would never have if you had a good working immune system that can be devastating in patients during immunocompromised. So, like I said any sign or symptom of infection I'd rather that you call me and me tell you that it's nothing. I'm probably not going to tell you it's something and probably going to make you get a bunch of bloodwork and get swabbed and get x-rays and come and talk to us but it's better safe than sorry because the things can really… especially opportunistic infections can just

really… (inaudible 33:12) very quickly in a matter of hours or days. I can't stress how important it is that you let us know when things are going on.

Q5: (inaudible 33:26)

Kelley Anderson, RN: Is he napping during the day? Yeah? That's probably our biggest culprit that I always feel bad taking away people's cat naps, but the biggest culprit for difficulty sleeping at night is napping during the day. Resting is fine, but even a 20 minute, 40 minute nap can totally throw off the circadian rhythm. So, trying to weaning him off naps a little bit, making the bedroom dark, light curtains that don't filter light in. Try not to bring devices to bed that kind of thing. Sometimes or there's some great… I use on Spotify has like a sleep setting. It's like soothing music help you sleep and I say it's like better than anything and (inaudible 34:22) light or white noise machines some people find helpful, but I think that probably if he's taking naps during the day that's… and it's a vicious cycle because you're taking naps during the day because you're not sleeping at night. Trying to find that one day to power through and get a good night sleep to reset that cycle.

Q6: (inaudible 34:45)

Virginia Klimek, MD: So, once the chemotherapy like the Vidaza or the Decitabine or the Revlimid or the anemia injections once they stop working and the evidence of that is usually the change in the blood counts for the worse. The anemia is getting worse, the white counts going down, etc. We do a complete disease reassessment. Just like when you were diagnosed. We go back in. We do another bone marrow. We see what's going on with the genetics, see what the blast count is and then we use all that information to say okay, we need to move in a new direction and we need a new treatment. What does the bloodwork and the bone marrow and all the genetics tell us about what the next step is? For many people that next step is a clinical trial because if you have low blood counts and increased blast counts once you've had Decitabine or Vidaza there's no other standard FDA approved treatment that will work in that situation. So, that's… in that situation you shouldn't be surprised to hear your provider start saying well, maybe you should go to Dana Farber or you should go somewhere… or I have a clinical trial available here. We should see if you're eligible for that. For some people that's the sign that it's time to move onto a stem cell transplant perhaps.

Q7: (inaudible 36:14)

Virginia Klimek, MD: Yes. Transfusions will work, but transfusions are like a band aid. They're not getting at the root problem inside the bone marrow. They're just trying to give you the cells that your bone marrow was unable to produce. So, it's going to have a transient effect. It's not going to fix the underlying problem, but for some people they can just receive transfusions and no therapy. In between transfusions they feel reasonably well. They're able to do most of what they want to do and you can go for a long time just on transfusions.

Q7: (inaudible 36:47)

Virginia Klimek, MD: Exactly. Exactly. Over time when the bone marrow function gets worse and worse and worse you… it takes more and more transfusions. The transfusions become more frequent and for platelet transfusions in particular you can develop antibodies as they call them where you don't respond to them anymore or as well. So, even long term transfusions have their limit.

Kelley Anderson, RN: Everybody's sleepy after lunch.

Q8: (inaudible 37:17)

Kelley Anderson, RN: I think you could… I mean…

Virginia Klimek, MD: I'm going to have Lea come over here. Could you ask that question again so Lea could (inaudible 37:54)

Q8: (inaudible 37:55)

Virginia Klimek, MD: Lea, can they print out what they generate to bring to the doctor or can…?

?: (inaudible 38:40)

Virginia Klimek, MD: Okay. So, there's going to be updates that will increase the utility and improve the functions?

?: (inaudible 38:52)

Virginia Klimek, MD: So, I think, of course, we want to talk about this app because the MDS Foundation. It's an MDS specific app, but just like the website you were highlighting. The Lots of Helping Hands. Like you said it's not… so, it's not MDS specific. So, please use whatever tools you can. If it's just a notebook that you keep and by the way I love it when my patients and their families keep a notebook. They bring it to every visit. They have all their information in there, all their notes and if it's your son coming with you one time and it's your daughter the next time they just pass the book between them. So, all the information is in the same place. If you have questions for the doctor you write them down. We really encourage people to use whatever whether it's pen and paper or an app to just try to keep track of your information. It's a very complicated disease. These are very complicated, difficult treatment plans that you're going through and whatever systems you can use to help keep things organized and make sure that

you're getting the information to the doctor and your nurse. Whatever works for you use it. Use it.

Q10: (inaudible 40:11)

Virginia Klimek, MD: So, this is a question that… the answer to this question has changed over the years. So, and the best data to answer that question is data that allows us to follow people for years and years and years. So, if you look at older data from like the 2000s when they were able to follow people for five and 10 years after transplant and you looked all comers with MDS at centers all around the country. That means different doctors, different ways of doing transplant and then you just took a snapshot of like how everybody… what the average outcome is. About 40 to 50 percent of people are cured and they're alive and doing well long term. That was… but a lot has changed in transplant to the point where we're using these reduced intensity transplants. We're doing T cell depletions. We're doing haplo cord transplant and we have better antifungal drugs, other medicines to treat infections and other complications – graph versus host disease. So, it's been sort of a dynamic process over the years that's improved transplant outcomes and so… but what I would emphasize is that in the modern era of doing transplants we also know that there can be a big difference in outcomes based on your genetics going into the transplant, how fit you are, what kind of donor you have, etc. So, you may… when you sit down with the transplant doctor and talk about what are my odds of being cured those numbers may be anywhere from 15 to 20 percent to 80 percent, but if you really… but the best data is this long term data, but it's kind of like false data and there's a lot of different types of people in that large group, but it's about 40 to 50 percent and that's based on something called the CIBMTR. It's a large intergroup transplant group data, registry data.

Kelley Anderson, RN: This was shared with me during lunch. An MDS support group and the meeting information. I'm going to leave it up at the front by the bags. So, if anybody wants to write down the information it'll be at RWJ Somerset Steeplechase Cancer Center and it looks like it'll be meetings the third Wednesday of every month with refreshments starting September 20 from 7:00 to 8:30, but I will leave this information at the front so that you can write it down.

Virginia Klimek, MD: And I think that Lea said that at the beginning of the meeting she announced that there was a support group starting up in maybe Summit, I think.

Q11: (inaudible 43:30)

Virginia Klimek, MD: The 19th.

Q11: (inaudible 43:44)

Virginia Klimek, MD: And that actually reminds that one of the questions that somebody had sent in ahead of time. I don't know if that person is here is or it was more of a comment saying

that it's useful for them to be around other people who have it to learn and share their experiences and these support groups are a great way to do it and I hope I'm not speaking… saying something wrong, but at least in the past I know that there's some folks at the MDS Foundation who are able to sort of help individuals to set up a new support group. If one of you were interested in starting a support group in your area… Oh, it's still correct.

Q12: (inaudible 44:24)

Virginia Klimek, MD: Okay. She doesn't want to say anything about it but it's true. But it's true.

MDS Foundation: No, feel free to contact us if you want to start one. Audrey (inaudible) a little bit of funding (inaudible)

Virginia Klimek, MD: Any other questions?

Q13: (inaudible 44:44)

Virginia Klimek, MD: Alright. So, we're going to go on. I have a few more slides. I wanted to kind of talk about some of the things that are being done in clinical studies, some new thoughts and discoveries related to some of the genetics in MDS and I know that, again, some of the questions that got sent in ahead of time there was a lot of questions about genetics. So, I don't know if you had some of your questions answered or if I don't answer them in this next segment please feel free to ask me.

So, you've heard me talk a lot about clinical trials. The importance of clinical trials is that we have a limited number of drugs that can treat MDS and really only one treatment that can cure it. So, we have a lot of work to do to find new drugs or new drug combinations to help improve quality of life and prolong survival and for people who have MDS and so the research efforts in a clinical trial setting, again, drug combinations and new drugs, but also I've mentioned some of these new transplant techniques to try to improve the access of transplants for people so that more people can have at least have the opportunity to have a transplant and also importantly because of this question that was just raised a few moments ago we know that MDS can come back after transplant meaning that there was just some little lingering amount left in the bone marrow that transplant wasn't able to eradicate and the disease can grow back and I'm just realizing now I didn't fully answer that question, but after transplant MDS can be very difficult to treat because the bone marrow is still very suppressed from the transplant treatment and by virtue of the fact that the MDS cells kind of survived all that chemotherapy and everything that came before it can be particularly resistant to treatment. So, that's another setting where clinical trials would be a reasonable option. On the other hand if somebody had a home run response to Decitabine before the transplant and then the disease came back after transplant it wouldn't be unreasonable to try that drug again just to see if it would work again.

So, this is a partial list of some of the new therapies and I say partial and let me see, one, two, three, four… 10 or 12 new drugs and this isn't even all of them. So, I want you to come away from this knowing that there's a lot of drugs that we're studying that we're trying to show will work and that are safe in MDS. There is an oral 5-Azacitdine drug that's being tested particularly in people with earlier or low risk MDS to try to see if we can try to treat earlier when patients are in a lower… have more low risk disease to see if we can improve how people feel and how long people live. There is a new drug that's being studied and it's looking very promising called Luspatercept. It's a drug that's specifically to treat anemia. It is one of the ones that I'm putting sort of on your watch list down here. These are the phase three studies. These are the drugs that are pretty advanced in terms of our testing and for you to keep an eye on because it may be that one of these drugs may be the next drug that's FDA approved for MDS. It seems the study that's going on right now as some of the people in this room know because they came to talk to me about this. It's not only an anemia focused drug, but it may have more preferential activity in people who have ring sideroblast type MDS. This Rigosertib is a drug that's been tested for many, many years and in a study that was called the On Time Study and I'm sorry I don't remember what the acronym meant. They were testing that drug in people who had Decitabine or Azacitidine and the Azacitidine and Decitabine had no longer worked. That's defiantly an area where we need new drugs and unfortunately in that study the survival of people who received that drug was no better than people who didn't receive it, but failure can be a good teacher. Right? So, they were able to go back and take a closer look at the people in that study and they think that they've identified a subgroup of people who may be more likely to benefit from that. So, Rigosertib is now being tested in a study called the Aspire Study and so what we'll hopefully we'll see if that drug given to people after they've lost their response to Azacitidine or Decitabine to see if that drug has a good response rate and if it prolongs the survival of people after they've been on the Decitabine or Azacitidine already.

This oral 5-Azacitidine is also in a phase three clinical study. This is in lower risk MDS. So, this will be exciting to see if the 5-Azacitdine is better than no therapy. So, I should say that this study, the Medalist Study and this Quasar Study are both comparing these new drugs to placebo. So, we'll be able to see if this drug is better than no treatment. The Rigosertib, by the way, is patients can be randomized to other treatment. There won't be a placebo arm in that study.

A lot of people ask me about immunotherapy. There is a lot of information out on television, in the magazines. You see the ads for it, for immunotherapy and we're testing immunotherapy in leukemia and MDS. So far they haven't worked so well by themselves in MDS, but they're starting… we're starting to do studies now combining it with Vidaza and with Decitabine. So, the jury's out a little bit on that so far. There are new drugs targeting things called CB47, CD138, whole life receptors. These are important proteins and pathways that control cell growth and differentiation in the bone marrow and so we're learning more and more about why people have MDS, what's gone wrong in the bone marrow and now we're able to find these targets that we can… and we can create drugs to try to fix that problem with that particular protein.

(inaudible 51:49) is a brand new drug that is we're actually testing it for the first time at Sloan Kettering in people who have MDS. It's a brand new class of drug that, again, targets… that tries to fix the way the cells are working so that it can promote normal growth of cells in the bone marrow. Thrombocytopenia is a big problem. We talked about it a little bit earlier. We really don't have good drugs to treat thrombocytopenia specifically. There was one drug. Some of you may have heard of it. It's the commercial name is called Nplate, N like in Nancy plate or Romiplostim. Has anybody ever heard of that? So, it's a drug that we tested years ago in MDS, but the reason you haven't heard about it was because we had to close all those studies down because there were some people on those studies when they were getting the higher doses and getting regular injections that and their disease turned into leukemia. They weren't sure if the injections were directly responsible for it, but when they did their safety evaluations they said you know what? We're not sure. Our first responsibility is safety. Shut down all the studies. So, we're not allowed to use that drug in MDS. However, there is a newer drug called Eltrombopag or Promacta. Has anybody been on that or heard of that? So, this is a drug that's FDA approved for a condition called aplastic anemia. That's one of those bone marrow diseases that was in that complicated ven diagram that I showed earlier. So, this is a… there are studies ongoing now with Eltrombopag or Promacta in MDS and it's looking very good. About 50 percent of the people who received this mediation, it's a pill, have improvements in their platelet count. So far we haven't seen any scary things going on with the blasts going up or people developing AML at a rate that's higher than would be expected. So, we've got our fingers crossed on that one and there are ongoing studies and this would be major because if you just have a low platelet count or a low platelet count is your dominant problem we really don't have anything to fill that slot. So, we're really hopeful that those studies will continue to show that it's safe and that it works.

This is something that's new in the past one year. So, I was talking to somebody at the break about ways to manage anemia if the Aranesp or the Procrit wasn't working. So, we've been talking also about… and you've heard me talk about Revlimid or Lenalidomide used by itself. So, some data emerged in that past year showing that people who were on Aranesp or Procrit shots. This is the shots that people take for anemia. If it doesn't work or if it stops working or if your doctor tells you that your EPO level is too high… Does anybody know what I mean by EPO level? So, forget about the EPO level part because that's… I don't have a slide to show you and I think it's best shown with a picture, but if you are on Aranesp or Procrit and it doesn't work or it stops working what these two studies showed this study here and the French did this group and then there was a United States group that did this. If you add in Revlimid you can recapture the response you had in the past or you can respond to the anemia shots like you never did before. So, if the Procrit or the Aranesp doesn't work this is what I would use as the next step. I would add the Revlimid alone and you can see that with these types of patients if they go on Revlimid alone versus Revlimid plus continuing the Procrit or the Aranesp your response rate is 39 percent compared to 23 percent. With this study the response was 25 compared to 10 percent. So, that's something that's relatively new and it's a little trick that we can use using drugs that are already FDA approved and available without going on a clinical trial.

And this is a really terribly busy slide and I was trying to pull this together. I am so sorry. This is a paper that I wanted to highlight. It came out of our group just a few months ago. Bart… I'm sorry… Bart Getta (sp? 56:27) is amazing doctor that came to visit us from Australia and he was looking for a project to do over years' time and so we put him to work and what he did was he went back to 2008 to 2015 and he looked at all the patients who we saw who had MDS at Sloan Kettering. We looked at the people who were medically considered to be a candidate for stem cell transplant and then we went back and just did all of these chart reviews and looked at all the lab studies and the bone marrow studies to see, okay, who went to transplant, who didn't and why not. Like who didn't… if you were eligible for transplant medically and you didn't go onto transplant why didn't they go onto transplant and what we learned was that there seems to be an age bias. What we found is that people over the age of 65 were less likely to be referred to a transplant doctor and if they were referred it took longer to get them to see the transplant doctor. As a result the people who didn't have a transplant most of them didn't have a transplant because their disease got the better of them and they passed away. So, mind you this is a study that spanned over a long period of time and remember I talked about the Medicaid ruling about five or so years ago. This also spanned the years that came before that. So, to some extent it's not the doctor's fault because there are other factors in play here, but we learned an important lesson and that is that you need to get people to the transplant doctors or at least get them considered… at least determined if they're a transplant candidate early and then if they are get them to transplant before their disease gets worse. So, in the end we found that only about 33 percent of people who we thought were eligible for transplant actually got one. So, I think that it's natural to sort of have this concern about age because, again, we want to cause more… we want to provide benefit more than harm and people worry that we can't do a transplant safely, but again transplant technology, techniques are improving and so that's the lesson that we learned and we got it out to the rest of the world about a month or two ago.

Genetics. Gene mutations. A lot of questions that got mailed in ahead of time were related to gene mutations. This was one of the first papers and this was in 2011. This was one of the first papers that came out and showed that even when you looked at a relatively small number of genes about half of the people had a gene mutation in addition to things like cytogenic abnormality. We also learned that if you had mutations in certain genes and I know somebody we were talking earlier about P53 we know that mutations in P53, EZH2 and these other three genes can be considered core risk meaning they change our perception about how you're going to do with your disease and we can use this information hopefully soon combined with all of your IPSS scores and your cytogenetics to help you to understand what's happing with your disease and the exciting part is that it's going to help us find new treatment. So, one of the genes that we learned a lot about in this study was a gene called SF3B1 and I know that some of you know about this because you've come up to me or you've asked me questions about this. SF3B1 was we discovered that that was one of the good ones to have. That was a good prognosis in a patient to have.

We've also learned about the differences in the mutations between different types of MDS. So, this was some data from my group studying therapy related MDS and leukemia. What we were able to show is that this TP53 mutation that you hear us talking about today and you'll probably read about is much more common in therapy related MDS compared to MDS that arises in people who never had another cancer therapy and so and you can see like in the TET2 mutations, this is another gene. It's much more common in de novo or MDS… when I say de novo I mean MDS that arises in patients who never had prior cancer therapy. So, you can see that there are differences emerging between different types of MDS based on their mutation analysis. What we're trying to do is take these differences, learn as much as we can about these mutations and how they're modulating your disease to try to help communicate to you about what's going to happen with your disease and also to develop new treatment.

This is that SF3B1 mutation I was talking about. This was first published also in 2011 by a group in Japan. They did some beautiful work here and the take home message for this slide is that these splicing gene mutations and SF3B1 is one of the splicing gene mutations. You'll hear that word a lot in the years to come can be seen in anywhere from 50 to 85 percent of MDS patients. So, these splicing mutations are going to turn out to be the most common mutation that we see in MDS and so stay tuned. We're going to be learning a lot more about these individual gene mutations and how we can capitalize on what we learn about them to develop new treatment.

This is a slide that I give to my doctor colleagues and I don't expect you guys to understand this, but this is a… what the take home message for this is that we're learning that as we get older we acquire mutations in our bone marrow. Remember I talked about earlier about how changes in your bone marrow as we get older it sort of sets you up to develop these diseases. This is what I'm talking about. This was a paper that was published in part by a collaboration with our colleagues in Canada and also at Sloan Kettering in 2012 and we were able to show that people over the age of 70 have this TET2 mutation, about 15 percent of people walking around with with normal counts and now we've discovered multiple other genes that are mutated in otherwise normal adults and, again, so I think this… understanding this biology of how we naturally age explains why this disease is happing in older adults and it may give us some clues eventually hopefully how to prevent it and predict to the development of these diseases.

We're also… and so this pheromone of having a mutation with normal counts, they've come up with a term for it. It's called CHIP, clonal hematopoiesis of indeterminant potential. What that means is you have a genetic mutation or a clone. It's there, but it's indeterminant in terms of what it means. We don't really know what it means. So, we're now coming up with these formal definitions of what CHIP is and now we're studying it and following people over long term to figure out what it means, but all this talk about mutations I just want to make a really important point and that is that at this point mutations cannot be used by themselves to establish a diagnosis and we're working on ways to incorporate mutations into these prognostic scoring systems. So, that time is coming when we'll be able to use them for prognosis and for establishing a diagnosis, but we're not there yet. One of the most common reasons that people come to me is

because they've had one of these fancy gene panels tested by one of their doctors and a mutation comes up and then the doctor doesn't know what it means and what to do and so they come to me and we have these long difficult discussions because now we have a test result basically an incidental finding with no disease and we don't know what to do with it. It's tricky. The technology is getting ahead of our knowledge of what to do with it.

Another thing that people as me is can my genetics, can my mutations tell me whether or not I'm going to respond to chemotherapy? Not yet, but there are papers that show that the TET2 mutation you have a certain TET2 mutation you may be more likely to respond to drugs like Decitabine and Vidaza with a difference of between 60 and 43 percent, but there's no difference In survival. So at this point whether you have a TET2 mutation or not we'll use these drug and hopefully we'll learn how to use these mutations to predict responses and duration of response in the future.

And I thought I had one more slide in here. What I will say is that remember that SF3B1 mutation I talked about, one of the splicing mutations. Just sort of as a peak into the future about two or three months ago a clinical trial opened up and it's at multiple centers around the country now with the first drug that's targeting SF3B1 mutations. So, this is how we do this. We learn about a mutation, we learn about what it's doing to the cells and then we build drugs to target that mutation, bring it into clinical trials. So, again, stay tuned because more of these drugs will be coming down the pike and hopefully we'll start having more drugs that are targeting these specific mutations.

So, yes. The company is H3 Biomedics and H3B8800 and it's a phase one study. So, they're just going through the initial dose of (inaudible 1:06:35) now. So, it's very early, but fingers crossed.

Q14: (inaudible 1:06:41)

Virginia Klimek, MD: So, splicing is happening in every cell of your body all the time. It's a normal way for your body to decide on a given day or given week what your body needs that week. You know how like electricians they splice, they opened up wires and they attach and reattach and hook it into outlets and things like that. It's the same idea. Your DNA is like a template, like a blueprint, but it's modifiable in the sense that you can use a short piece of DNA or a long piece of DNA depending on what protein your body needs at a given time. So, splicing, cutting it either short DNA either short or a long piece to make a protein depends on what your body needs. So, it's a normal part of your daily body function, but what happens is that if you have a mutation it's not splicing correctly and it's making the wrong protein at the wrong time, too much or too little of it. What these drugs are going to try to do is just restore your normal DNA slicing program and that's reasonably (inaudible 1:08:13). It's complicated (inaudible).

Q15: (inaudible 1:08:18)

Virginia Klimek, MD: We won't know if it's a cure or if and… first of all we don't get how well they work or how long they'll work, but for example Kelly showed a slide of somebody who was on Revlimid for 10 years. I have somebody who's been on since 2003. She's on Revlimid and she's doing fine since then. Even if it doesn't cure you if it's a pill that you have to take every day like your thyroid medicine or your heart medicine maybe a cure isn't what's needed, but it's way too early to know that. It's way too early.

Q16: (inaudible 1:09:02)

Virginia Klimek, MD: Ah, (inaudible 1:09:30). I think you're talking about CAR T cell.

Q16: (inaudible 1:09:32)

Virginia Klimek, MD: Yeah. It's really exciting stuff. It's really exciting stuff. Yeah. I mean, I just treated…. We were just treating with multiple myeloma with CAR T cells the other day. So, what they do and that's not ready for… we're not doing that in MDS. Maybe we will at some point, but we're not doing that in MDS, but…

Q16: (inaudible 1:09:52)

Virginia Klimek, MD: Yes. So, there are CAR T cells where car T cell programs that are used to treat certain types of leukemia and multiple myeloma, CLL, is another type of leukemia, a low grade leukemia and they're genetically modifying the T cells to recognize the cancer cells so the T cells go in and attack the cancer cells.

Kelley Anderson, RN: On Sloan Kettering's website if you're interested there's really, really, really good information that was like how I learned about it was like on our outfacing website. It was like… it was very cool.

Q17: (inaudible 1:10:29)

Virginia Klimek, MD: It's more of a neutral one.

Q17: (inaudible 1:10:43)

Virginia Klimek, MD: Yes. I will tell you that when we first saw those TET2… So, we knew about TET2 mutations before we discovered them in normal people and we said, ah ha. If you have a TET2 mutation and potential thromo(inaudible 1:11:16) or myelofibrosis or MDS it must be linked to disease. I mean, that was like the natural connection, but then once we found it normal people with normal counts that was a real eye-opener because it told us some of these mutations are just sort of along for the ride. We call them passenger mutations because they're just there. They're not doing anything. They're not driving the disease. They're sort of

passengers. So, it really gave us pause in the field that we had to be more careful about what we say these mutations mean and so now we're finding that people with normal counts otherwise healthy can even have mutations in P53. I could have a mutation in P53 with normal counts. I don't know what it means for me down the road. ASXL1, DNMT3A, SF3B1 mutations. We're finding all these mutations in people with normal counts. It remains to be seen what it means for those individuals as time goes on.

Q18: (inaudible 1:12:23)

Virginia Klimek, MD: We can generally pick those up in bone marrow and blood, but I would not recommend going and asking for that test because…

Q18: (inaudible 1:12:43)

Virginia Klimek, MD: Because we wanted… because we were trying to understand the biology of the mutations in the blood in general and the bone marrow in general. It was part of a research study. It was part of a research study and then, of course, when they started finding these mutations then they really started expanding and looking at more and more people who had normal counts.

Q19: (inaudible 1:13:15)

Virginia Klimek, MD: So, the list of suspects, the types of mutations in MDS have grown and there are... so first of all there's a lot of growing literature kind of describing them and talking about them and exploring what they mean and how they contribute to the disease, but maybe rephrase your question. I'm not sure I'm answering the question.

Q19: (inaudible 1:14:08)

Virginia Klimek, MD: Oh, got it. Do you know what lab it was done at?

Q19: (inaudible 1:14:30)

Virginia Klimek, MD: Most laboratories have really gone to a lot of trouble to include in their reports and these reports end up being like 20 pages long. I mean, they're really long where they'll… let's say if you have three or four mutations they'll describe them, say exactly where they are in the gene because there's different places in the gene that a mutation can occur and then they usually provide the information. They'll say this has been associated with XY diseases and these are the clinical trials that are currently available to target them. So, some of the annotation that come with these reports are really, really good. Yeah.

Q19: (inaudible 1:15:14)

Virginia Klimek, MD: I know like Foundation One does really good reports. GenOptics I think does. GenPath is the lab does them. I just don't remember their report format.

Q19: (inaudible 1:15:28)

Virginia Klimek, MD: Our in-house… we have an in-house panel that we do. We don't send it out and we do all of our work in-house. Our in-house reports are not as well annotated as Foundation One or like GenOptics because they think I'm qualified to interpret it. I'm laughing because I just realized it. Just as you asked me that question I'm like oh, yeah. That's right because they assume I know how to interpret it.

Q19: (inaudible 1:16:02)

Virginia Klimek, MD: But that's what I think is really helpful for individuals and their providers to be able to say okay the field is moving so fast. We're learning. Things are changing so fast. We need that information from the specialists who are doing the test to help guide us and I think that's why I get a lot of consults from people who have these mutations because a lot of times we're doing these tests are being done and we don't know what to do with the information.

How are we doing? Are you ready for the quiz? Oh, you're welcome.

(Applause)

Thank you very much. Thank you.