

Speakers:

Virginia Klimek, MD

Jayshree Shah, APN-C, MSN, RN, BSN, BS

Jayshree Shah: We have about an hour's worth of time left together today and I just wanted to leave this time for you as patients, caregivers, supporters of MDS. I want to just give this one hour to you guys to ask any questions for myself related the presentations that were done, if you had specific questions related to that or just in general and Dr. Klimek is also available to answer questions with me. I thank her for staying and being part of this entire day. This is great. So, I leave the floor to you. This is an open forum and we are recording. So if you can I'm going to pass this mic along to the first person that asks the question so that it passes along to the second person and I would like you to speak slowly and clearly please because your questions mean a lot and since we are recording to transcribe it and put it on our website for future documentation and if people want to review it or go through it, if they want to learn more about MDS. So, this is used as a reference. About 1:30 Debra is going to pass around a survey for the day. Feel free to write any comments, anything related to today's discussion or something that you may be interested in learning for the next round. We're hoping to hold another session hopefully next year again here. So, feel free to write any comments or suggestions because, again, we're always wanting to improve and have these sessions available, so we learn and we share because that's what you guys are here for. Again, my name is Jay. People call me Jay. I mean, the full name is Jayshree. I just cut it short now. Feel free to, again, go forward. So, who's going to be the lucky one to ask the first question? Again, speak clearly and slowly please.

Q1: My sister-in-law went for a bone marrow transplant because it was so painful... bone marrow biopsy because it was so painful and she was jumping around so much, they only got fluid which is not definitive as the bone marrow. Why can't they sedate you? They keep telling her no. They won't sedate here and she can't face another one.

Jayshree Shah: So, it depends who's doing the procedure. Is it jumping around because you were jumping around because...

Q1: Pain.

Jayshree Shah: Pain. Even the Lidocaine.

Q1: So, would sedation contaminate the bone marrow that's why they...?

Jayshree Shah: No. There are ways of doing bone marrow sedation biopsies. It's a step process like any other procedure where if you want to kind of put a person under lightly under... like a nice sleep. Something like that. I think you may have to have that discussion with your physician and say, "You know, I need your help to help me find somebody that be willing to do it." I think if you have that open conversation, it may take a while, but they'd be willing to set this up for

you and, again, you may have to get some clearances and whatever to go forward to doing that. It's a pain in the butt. Literally.

Q1: Is that fluid not as telling?

Jayshree Shah: It depends on how much the fluid, where they sent it, what they sent it for. I think if the information that they were seeking was just from the fluid alone, again, you have to have that discussion with your physician and ask him the fluid that you collected, the sample that you collected, was that enough for what you needed and what are you testing for? The more questions you ask to your physicians and nurses whoever is taking care of you, the more information you will get back. What I tell my patients is when you go to a doctor's office, you want to be prepared. When you go sign for a house when you're signing your closing, you have to have your documentation, boom, boom, boom, boom, boom. You got to get your bank statements, approval and a check and all this stuff. It's the same concept when you go to the doctor's office, bring a notepad. Write down your questions beforehand. Have a thought process and saying, "You know what? What are the top three questions that I'm going to ask my doctor today?" or, "ask Jay today." "Jay, what is my level for," I don't know, "vitamin B12 that was drawn last week? I need to know whatever and I want you to explain what it is." Stuff like that. Just write it down, so you don't have to think about it. All you have to do is, of course, put that piece of paper in your purse or your back pocket or wallet or something. I suggest that because when you go to the doctors, I think for myself and others, they always feel like there's this wall like they go there and they are listening, listening, yes, yes, yes, nodding away and they leave and they have five other questions. I get a phone call back later for the end of the... or the next day. "Jay, I forgot to ask you this." So, that's helpful and also always bring your medication list. Herbs, vitamins, supplements, anything that you take over the counter plus your prescribed medications. Write it down on a piece of paper. It's very helpful and it makes it very easy for your healthcare practitioner to know Jayshree's taking A to Z. Now, I know what I'm dealing with if I want to prescribe this for her versus me grilling you, "What did you take? What pharmacy did you use?" I have five different pharmacies. Well, okay. That's fine, but that means I have to step away and get all that information and it takes away my time from you.

The next question, pass the mic along.

Q2: So, we're in the position of perhaps having to start Revlimid in our future. So, the questions about that. What are typical responses to Revlimid? What are typical benefits over time of it with a 5Q issue and then the same question for growth factors?

Jayshree Shah: Revlimid is, let me go back it up. It's a treatment modality that Dr. Klimek actually explained and talked about very briefly for patients with MDS. It is used for MDS patients as well as patients who have a specific mutation. A little break in the DNA it says, "Oh, you know what? I feel like breaking and making this mutation called 5Q deletion." You probably think, "Jay, how do I know if I have it?" That's the conversation you need to have with your

physician and ask him and say, him or her, and say, “Can you go over my cytogenetic report?” With the liquid that was collected for your sister, the information we were seeking is information such as cytogenetics which is what her sister made of right now, not 20 years ago, right now. Has she developed mutations now? She develop any preleukemia cells right now and does it have 5Q deletion? That’s the information from the liquid. For Revlimid, if you have that 5Q deletion, it’s a specific treatment modality that we’ll study to use for those patients and it proved efficacy. Efficacy enough that the FDA said, “You know what? This is important. It’s worked.” Worked in a sense where it actually for patients who had it the MDS and 5Q deletion, patients became transfusion independent. Their anemia levels, or anemia, resolved. Not for everybody over time. There are rules with starting... when you take this medication that the patient will have to follow by monitoring the blood counts on a weekly basis counts times at least eight weeks if not more and supporting them while the MDS is changing within the bone marrow, supporting them with blood products, platelet transfusions and other treatment dates such as growth factors possibly because the patients can become very neutropenic. Neutropenia is white blood cells. So, you have to be very careful of balancing all those things. So, we’re dealing with platelets, white count and hemoglobin. So, monitoring all that throughout the treatment process of being on Revlimid is very important, very critical. Patients can bleed, develop infections and become very, very fatigued enough that they may not want to get out of bed and also possibly develop blood clots. All those things component they come in...

Q2: Tell what? I didn’t hear.

Jayshree Shah: Blood clots. So, that’s what’s being used for that specific reason. The side effects... Do you want me to review those side effects real quickly in regards to?

Q2: Do you have patients who’ve been on Revlimid? Do people stay on it for any length of time and over time, what is the experience of folks and does the benefit continue?

Jayshree Shah: Sure. So, it goes by the patient’s initial diagnosis of having MDS with where they are with their MDS. Do they only have 5Q deletion that we’re dealing with or are we dealing with 5Q deletion and five other mutations? So, that conversation you need to ask your physician meaning ask that question to your doctor and say what are we dealing with? As far as the numbers of how good it’s going to work it depends on that mutation line how many.

Q2: Have you had patients on Revlimid and what is their actual living experience of being on this and being on this all the time?

Jayshree Shah: So, I’ve had many patients being on Revlimid and they done actually well while they are... for thi treatment modality, for specific 5Q deletion. We’ve also used it for patients with 5Q deletion plus other mutations. Those patients are different setting, they’re different indication. They’ve done well. They can stay on it. We have also used Revlimid at different dosages at different times. So, some patients I’ve used, just for example, every patient is

different now. One patient I've had to use Revlimid on every third day. You probably saying, "Jay, it says every day to give it every day." Well when I gave it to the patient, her numbers... her side effects that she was experiencing was too much. So, it's a balance of her side effects with the numbers and how she's feeling with the quality of life. So, we take a look at the whole picture. I think what I would suggest is if that therapy is being used or considered for whoever, I would say write down your questions that you're asking that to me and to the rest of the group to definitely discuss it with your physician but to give your perspective it is a pill form therapy. It's not immediate therapy that will resolve and take away, but you definitely need resolve meaning to take away and say bye MDS forever. Will they need to stay on this medicine forever? Probably until it stops working and then maybe something else will come about.

Q2: Thank you.

Q3: I've been Revlimid for two and a half years at least, 7 ½ milligram and I haven't had one side effect from it at all, but I do have to go every (inaudible 13:29 – 13:32) six months is long enough to. That's what I've felt. At that time I said it doesn't seem to be doing me any good. Just like Dacogen.

Jayshree Shah: Dacogen. Decitabine.

Q3: Again, nine months on it and having really severe reactions after the seventh and eighth month.

Jayshree Shah: Dacogen is a hypomethylating agent or Decitabine and that was one of the treatment modalities that Dr. Klimek talked about where you take away the extra methyl from the DNA and say, "Okay DNA, work properly now." So, you need a hit, a hit to the bone marrow and the DNA every month from the Dacogen to take away the extra methyl. If you don't get that hit then the bone marrow says, "Oh. Well, I'm going to keep on making the extra methyl," and hence the disease may possible progress. So, it's a balance of treatment option available, discussing it, telling your patient or discussing it and telling them this is a lifelong process and it's a commitment and to be very patient. It's not like solid tumor world where if you see that tumor and it shrinks and it's gone, it's gone. This is different and this is we're dealing with blood and you can't feel it unless you poke somebody and the person's actually bleeding. So, you don't feel it and it's different to conceptualize that people have this. So, that's what makes it difficult.

Q4: When you mentioned bleeding, infection, blood clot development that... those were signs that would require you to have Revlimid and I think I missed the fourth or that's the aftereffect of having it or...?

Jayshree Shah: No, those are the symptoms that you want to monitor while being on Revlimid.

Q4: It was a fourth and I don't remember...

Jayshree Shah: White blood cell. So infection, anemia, checking the CBC for blood counts meaning hemoglobin and also platelets for bleeding.

Q5: Hi. I was just wondering if you could speak a little bit on the side effects and the risks of the hypomethylating agents.

Jayshree Shah: Sure. So, hypomethylating agent is, again, used as a treatment modality for MDS patients as one of the options. There are two right now that are available on the market. One is Azacitidine. This is, again, the other name is Vidaza and it can be given in different time, five days, seven days. Five days, six days, whatever your doctor decides is fine. The other drug is Decitabine and the other name for it is called Dacogen. They both are sister drugs, but their chemical compounds are a little bit different in the way chemistry if your formula looks like. People experience different side effects for each one. So if I asked (Attendee) what her side effect for Dacogen versus (Attendee), sorry, making up a name here, (Attendee). (Attendee) had... every person will react in a different way, but it also goes with the type of MDS a patient has, where they are with their MDS. That's also critical. How you choose treatment modalities is a discussion you need to have with your physician and ask him the question why would you choose this one versus the other. The side effects that I tell my patients to review I discuss with my patients when we're about to decide which one and say we decided Vidaza or Azacitidine as a treatment option and if we're planning on doing subcutaneous injection versus IV, obviously, it's going to be localized, redness, some pain associated with the injections. As far as side effects, you may have some a little bit of nausea, constipation because I'm giving you a nausea pill to prevent nausea, but as a side effect from that pill is the constipation. Dacogen is a similar effect. So with MDS, if you think about it and just picture yourself as with MDS as a garden, let me start there, where it's filled with weeds, completely, maybe not completely. Ninety-five percent and there's five percent that's good. That's a nice little corner patch left where you had planted the tomatoes. That's growing nicely. Leave it alone, but 95 percent of your garden is covered with weeds. When you're getting Dacogen or Vidaza and you're trying (inaudible 18:45) hit with it. That's a weed killer. We're calling Vidaza and Dacogen the weed killer. Hit meaning the five days of therapy of the Vidaza or Dacogen will not clear the 95 percent. That's why you need a hit every month to five weeks depending on, again, your treatment plan that's decided to take away the weeds and when the first hit comes, the hit is strong because the body doesn't know how to react and with that hit the counts go down. Patients feel tired, more tired than usual. I tell my patients all the time when they have MDS be patient. It's going to take up to four to six months before you start feeling some difference and you're saying people are... my patients always tell me, "Jay, that's a long time. You're talking almost springtime now." You're going to have to be patient until we start seeing the numbers go up and you start feeling better and you become transfusion independent.



Q5: Is there any chance that once those numbers go down they do not rebound?

Jayshree Shah: They do... Well again, it depends on the type of disease and where they are. Sometimes when the counts go down it's a balance of knowing when to intervene whether... what cytopenia you're dealing with. Are you dealing... talking about the neutropenia, hemoglobin or platelets. Neutropenia they may need a little growth factor support to say let's go, bump it up... bump up the engine.

Q5: Neulasta.

Jayshree Shah: Neulasta it depends, again. My rules are different for utilizing Neulasta. I tend not to because their half-life is longer than a little touch of Neupogen, but also there's rules of when to use it and when not to use it. So, and hemoglobin if it's low, obviously, we have blood products to transfuse if the patient is willing to go forward and platelets, again, they're readily available, but they die off in three days. So, you have to be careful of when you transfuse and people develop antibodies after many transfusions, so that's also a concern.

Q6: My whole side turned black and blue just about and I thought it was because you hit yourself and you fall and so I didn't pay any attention but then when I went to the doctor, I wasn't even home yet and he called me on the phone because he had me go for a blood test and he said, "I want you to come to the hospital right away and I want somebody to drive you because..."

Jayshree Shah: Maybe it was ITP.

Q6: I don't really know what...

Jayshree Shah: If you know... thrombocytopenia purpura. So, our immune kind of trigger that can happen in your body to say I want to just wipe out all your platelets from the garden, just wipe it out and, hence, maybe that's why you saw the black and blues and...

Q6: My whole chest, my arms. I didn't pay any attention because, you know, I'm doing lawns and climbing trees and everything. So, I figure I hit myself.

Jayshree Shah: It sounds like something similar to like an autoimmune kind of a component where your body just decided at some point to say I want to just knock out all the platelets from the bone marrow and just knock it out of the system and Prednisone is a steroid that you use as a treatment for modality for that type of autoimmune disorder.

Q6: They don't use it for the MDS.

Jayshree Shah: We do.

Q6: They do?

Jayshree Shah: We do in a different way... in a different way, different dosages for different reason, different type.

Q6: I was on it for about two years I would say (inaudible 22:48) Prednisone and cut down... and you have to cut down slowly.

Jayshree Shah: It sounds like it is, but again I think the best person to answer that would be your physician.

Q6: I never thought to ask him because he was the same physician then and then 20 years later I lucked out and my primary physician sent me to him and it happened to be the same doctor. So...

Jayshree Shah: That's interesting.

Q6: He's great though, I must say.

Jayshree Shah: Yeah. Well, you're still with us. Right?

Q6: Right.

Jayshree Shah: There you go.

Q7: Following up on her comment. Where do you use Prednisone in MDS?

Jayshree Shah: It depends. Sometimes we use it as a treatment... part of the treatment in conjunction with an agent. Sometimes we use it alone and it's a steroid. So, we use it sparingly and sometimes we have a... I've taken care of few MDS patients where they've actually had autoimmune component plus MDS. So, it's a balance of the autoimmune keeping it suppressed, the issues of the patient having a symptom or a side effect or something with a low dose of something, Prednisone plus giving them hypomethylating agent to keep everything balanced. It's about a balance at the end of the day of whatever type of MDS that the patient presents with and trying to figure out a recipe of weed killer, different types of weed killers for that person.

Q8: I have (inaudible 24:29) Procrit.

Jayshree Shah: Yes. Procrit. What about it?

Q8: What's the point of it?

Jayshree Shah: Procrit is a growth factor in a sense where it helps to stimulate and tell the kidneys and the bone marrow to say let's turn it up. Turn up the red blood cells and so we can have more energy and it's to use as a treatment modality for patients who have MDS. Yes, Dr. Klimek. Go ahead.

Virginia Klimek, MD: So, Procrit is a medicine that it mimics a natural substance that your body normally makes. So if you know anybody that has, for example, like thyroid disease or diabetes, you take medicines to replace what your body is not able to produce like thyroid hormones or insulin. So, the Procrit is just a synthetic version of a natural substance that we all make in our kidneys and I always describe it to my patients as it's like you know how I described the bone marrow as a factory. Well, the Procrit is like the foreman. It circulates around in the blood and when it gets into the bone marrow, it's basically telling the bone marrow work harder, make more cells. It's like cracking the whip on the bone marrow. So, what it's doing, it's not fixing the bone marrow. It's not getting at the root problem, but it's making whatever bone marrow... make blood cell ability... making ability your bone marrow has it's making it just work harder and it can increase the hemoglobin. In some people it can reduce or eliminate the need for transfusions and sometimes we find it's really an important part of the treatment for people who have MDS if they have underlying kidney problems because that substance, the natural substance I told you about, most of it's made in the kidneys. So, there's an instance where an individual person, their management might be changed by the fact that we know that in addition to MDS they have kidney disease. So, they're going to be maybe more likely to benefit from those Procrit shots.

Q8: She gets a regular one every week, but for the last three years. Is it an indefinite type of drug?

Virginia Klimek, MD: It's used indefinitely as long as we think it's providing benefit. As long as your doctor thinks it's working, you can use it indefinitely. At some point if you feel it's not working then it should be stopped, but that's going to be up to your doctor to decide.

Jayshree Shah: Alright. We got a couple more questions.

Q9: This is easy.

Jayshree Shah: Okay. Go ahead.

Q9: If once you've stopped taking Procrit because it was found to be ineffective, do you recommend trying to get back on it and see if it's now producing the task it was designed for?

Virginia Klimek, MD: So, there's a couple situations where I might make that recommendation. One is where let's say... let's say you were on Procrit. It was working for a while and then it



stopped working but then you developed kidney... getting back to that kidney thing, you developed kidney problems and you're not just able to make even the amount that you were able to make before. I might try it again to see if we can boost those levels up to kind of replace what your kidneys were doing. That's number one. Number two, if you're on those shots, they don't work anymore, you stop them and then down the road you go on something like Vidaza or Decitabine, if you remember the Procrit I said, the Procrit and the Darbe shot, they don't fix the bone marrow, but the Vidaza and the Decitabine, they actually are weed killers. They can actually get rid of the bad cells and help promote the bone marrow to work better. So, those drugs are getting at the root problem in the bone marrow. So if you can imagine if you've gotten rid of the weeds and you're trying to grow blood cells, red blood cells, throw in some fertilizer and that's kind of what the Procrit will do. It will help kind of stimulate the normal cells, help the normal cells to come back. So, it's different now because the Vidaza or the Decitabine has changed the bone marrow in a way that might make it more receptive and maybe more able to respond to the Procrit. So sometimes I reintroduce the Procrit later even if it didn't work before because the bone marrow itself is working better and it may be able to respond and so sometimes I can improve the hemoglobin even beyond what the Decitabine or Vidaza is able to do by just adding back in the Procrit or the Darbepoetin.

Q9: Thank you.

Q10: Dr. Klimek, based on what you just said would nephrologist actually use Procrit for patients who have like 30 or 40 percent deficiency kidney?

Virginia Klimek, MD: Yeah, they do. It's and anybody who's on dialysis is automatically receiving it as replacement therapy basically. Yes. So, renal failure or kidney failure is another reason. It's marketed under a different name.

Q10: What's it called?

Virginia Klimek, MD: Epogen.

Q10: Ebadin?

Virginia Klimek, MD: Epogen. It's the same, but it's the same... It's the exact same thing as Procrit. That's why you don't hear it talked about in the context, Procrit, talked about in the context of kidney failure.

Q10: Is it typical to use Procrit even if you're natural EPO levels are normal?

Virginia Klimek, MD: That's a really good question, but it'll help me to prompt me to explain something about the way that we use it. So, let's assume you have normal kidney function. Your kidneys are chugging along. They're making all this stuff. It's doing... Your body is doing what

it's supposed to do and when your body is doing what it's supposed to do, when you're anemic the kidney sense it and it makes more. So, your levels of that natural substance should go up. That's the natural reaction, but what we found out is that when we grow bone marrow cells from people with MDS and aplastic anemia in the laboratory, they need higher than normal levels to grow. So before your doctor starts Procrit or Darbepoetin in you or Aranesp, we check that natural EPO level. Even if it's very high, we may still think the people can still benefit from the Procrit or the Aranesp on top of what they're already making and even if... So, even if it's very high because we know that we have to kind of get it super high for the bone marrow to respond. So, yes.

Q11: Have you ever (inaudible 31:24) people going into remission?

Virginia Klimek, MD: Oh, yeah. Yeah. Remission. Yeah, yeah. Yes.

Q12: What was the question?

Jayshree Shah: The question was have you had experience with patients going into remission?

Virginia Klimek, MD: But there's a difference between remission and cure.

Q11: Right.

Virginia Klimek, MD: So, I have people in remission of Vidaza. I have people in remission on Decitabine. I have people in remission on Revlimid. I don't have people in remission on Procrit or Aranesp even if their hemoglobin is normal because know that the MDS is still there, but we're just making the bone marrow work harder to compensate.

Jayshree Shah: If you forgotten any or you think of any other questions, feel free to reach out to MDS Foundation. The books that you guys have are a great resource and in regards to learning about the disease, sharing it with other people that want to know about the disease and utilize the MDS Foundation website please. Feel free to use it. Again, support us. We want to grow as a foundation and share knowledge with others about it and thank you so much for coming. Yes, (Attendee).

Q13: We should get Robin Roberts who was so well known. She is always touting the implant part but she never discusses the disease that created the need for the implant. I mean, here is someone who can really do something. She has that celebrity, but she has not. If you saw her up here and she talks about it, but this is where it could be and Nora Ephron is dead, but people are not aware that Sagan, Carl Sagan and what's her name? Susan (inaudible 33:18), but Roberts, she has a lot of celebrity power.

Jayshree Shah: I think I'm going to make my phone call today to her.

Virginia Klimek, MD: But I also think that she's also trying to be an advocate for another unmet need and to try to make sure we have as many donors as possible.

Q13: For the implant.

Virginia Klimek, MD: For the transplant, yes.

Q13: Sure. That's what she promotes.

Virginia Klimek, MD: Yes, yes because that's what worked for her and she's a celebrity, but I think she's also a human being and so I think...

Q13: But that works for her, but she had the disease and that's... you want to have the visibility.

Virginia Klimek, MD: Sure. Sure.

Jayshree Shah: She does talk also about MDS.

Virginia Klimek, MD: She is doing a lot as well for the transplant part. Yeah.

Q14: After you have a transplant, is she cured or just in remission?

Jayshree Shah: You're considered cured after five years. I think she's still in that phase of yes she's been past 100 days after transplant. Remember the transplant doctor went over the zero is her birthday for her transplant. Counting from there to 100 days thereafter is a critical point because they do a repeat bone marrow then. Thereafter, they do repeat bone marrows at one year, two year, three year, whatever her oncologist has designed the plan for her. At five years there forward if everything is negative then yeah. She's considered cure.

Q13: I propose a visit. If Nora Ephron's son was on TV, two programs, and he spoke about MDS. Well, of course, because she didn't get the transplant. I don't think so. I don't know whether that was the... but he doesn't have that celebrity power that she's on all the time. She could raise money for us.

Virginia Klimek, MD: No and know, but unfortunately also it's MDS as I pointed out, it's a relatively rare disease, too. So...

Q13: That's why you need her.

Virginia Klimek, MD: I know. I know. I know. I know.

Jayshree Shah: Yes, ma'am. Go ahead.

Q15: Yes. I've been talking to Dr. Klimek and Audrey (inaudible 35:28) from the foundation about having the support group in New York City and so we were talking about sending out some kind of mailing about that to try to organize that. I don't know... We're really not sure if... I mean, it would be... it depends on whether people feel that that would be useful to them and how it would be useful. It may be that the differences don't make it so, but maybe it does. We're going to try to do that.

Jayshree Shah: So, that's a great idea. So, that's another reason why we have these patient forums is ideas such as those are important to share and consider and to talk about and it gives you a great avenue to give your phone number to her, E-mail to her and others to share and start the support group that by next year maybe you guys will start it and it'll grow to fruition.

Q15: I'd be happy to take anyone's E-mail address or phone number or something, so I can share information.

Jayshree Shah: And we could start the process now. Yeah. Yes, ma'am.

Q16: I'd like to point out that the incidence of MDS will be going up because right now it's rare, but you have an aging population that's living longer than we used to and you also have everyone getting cancer and being treated for it.

Jayshree Shah: In some form or something for some reason, yes.

Q16: It's going to go up.

Jayshree Shah: That's a very good point.

Virginia Klimek, MD: I agree and I... I agree with you completely. We think that there's also an incidence, a rising incidence in this therapy related type MDS because the better we get at curing other cancers and the longer people are living and surviving their other cancer, we're definitely going to see more of that and that's another reason to study that problem. It's terrible when that happens, but obviously you need to treat the other cancer, too.

Jayshree Shah: We have lots of food available still. Feel free to grab a bite on your way out or take it with you. One last thing. If you can please hand in your surveys to Debra, myself, Audrey. If you finished, just because we, again, want feedback so that we can improve and make the suggestions, changes, to the next patient forum. Thank you so much all for coming.

(Applause)